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权利要求书5页 说明书57页

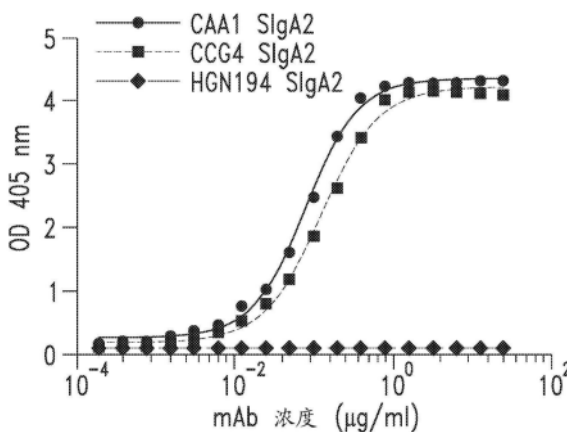
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(54) 发明名称

针对弯曲杆菌物种的抗体

(57) 摘要

本公开内容提供了对弯曲杆菌具有特异性并且在某些实施方案中,能够中和对象中的弯曲杆菌感染的抗体及其抗原结合片段。在某些实施方案中,所述抗体或抗原结合片段包含IgA抗体,诸如例如分泌型IgA抗体。还提供了包含公开的抗体或抗原结合片段的药物组合物。还提供了使用所述抗体、抗原结合片段和组合物治疗或预防对象中的弯曲杆菌感染的方法。在某些实施方案中,将本公开内容的重组分泌型IgA抗体口服施用至具有弯曲杆菌感染或处于发展弯曲杆菌感染的风险中的对象。



1. 分离的抗体或其抗原结合片段,所述抗体或其抗原结合片段对弯曲杆菌鞭毛加帽蛋白(FliD)表位具有特异性,所述抗体或抗原结合片段包含(i)分别如SEQ ID NO: 9-14所示的HCDR1、HCDR2、HCDR3、LCDR1、LCDR2和LCDR3氨基酸序列;或者(ii)分别如SEQ ID NO: 25-30所示的HCDR1、HCDR2、HCDR3、LCDR1、LCDR2和LCDR3氨基酸序列。

2. 如权利要求1所述的抗体或抗原结合片段,其中所述表位是构象表位。

3. 如权利要求1所述的抗体或抗原结合片段,其中所述表位是线性表位。

4. 如权利要求1所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段能够通过ELISA测量的小于0.1 $\mu\text{g/mL}$ 、或小于0.05 $\mu\text{g/mL}$ 、或小于0.03 $\mu\text{g/mL}$ 的EC50结合所述FliD表位。

5. 如权利要求1所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段能够在体外细胞运动性测定中降低所述弯曲杆菌的运动性。

6. 如权利要求1所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段能够中和对象中的弯曲杆菌感染。

7. 如权利要求1所述的抗体或抗原结合片段,其中所述弯曲杆菌包括空肠弯曲杆菌(*Campylobacter jejuni*)、大肠弯曲杆菌(*Campylobacter coli*)或两者。

8. 如权利要求1所述的抗体或抗原结合片段,其中所述弯曲杆菌包括空肠弯曲杆菌81-176、大肠弯曲杆菌10092/ATB或两者。

9. 如权利要求1所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段包含:

(i) 与SEQ ID NO: 2具有至少85%的氨基酸同一性的VH以及与SEQ ID NO: 4具有至少85%的氨基酸同一性的VL;或者

(ii) 与SEQ ID NO: 22具有至少85%的氨基酸同一性的VH以及与SEQ ID NO: 24具有至少85%的氨基酸同一性的VL。

10. 如权利要求9所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段包含:

(i) SEQ ID NO: 2所示的VH以及SEQ ID NO: 4所示的VL;或者

(ii) SEQ ID NO: 22所示的VH以及SEQ ID NO: 24所示的VL。

11. 如权利要求1所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段是IgA、IgG、IgD、IgE或IgM同种型。

12. 如权利要求9所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段是IgA、IgG、IgD、IgE或IgM同种型。

13. 如权利要求10所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段是IgA、IgG、IgD、IgE或IgM同种型。

14. 如权利要求11所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段是IgA同种型。

15. 如权利要求12所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段是IgA同种型。

16. 如权利要求13所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段是IgA同种型。

17. 如权利要求14所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段是IgA1同种型。

18. 如权利要求14所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段是IgA2同种型。

19. 如权利要求15所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段是IgA1同种型。

20. 如权利要求15所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段是IgA2同种型。

21. 如权利要求16所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段是IgA1同种型。

22. 如权利要求16所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段是IgA2同种型。

23. 如权利要求1所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段包含Fc多肽或其片段。

24. 如权利要求9所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段包含Fc多肽或其片段。

25. 如权利要求10所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段包含Fc多肽或其片段。

26. 如权利要求23所述的抗体或抗原结合片段,其包含与SEQ ID NO: 40-42中的任一项具有至少90%同一性的重链恒定区。

27. 如权利要求24所述的抗体或抗原结合片段,其包含与SEQ ID NO: 40-42中的任一项具有至少90%同一性的重链恒定区。

28. 如权利要求25所述的抗体或抗原结合片段,其包含与SEQ ID NO: 40-42中的任一项具有至少90%同一性的重链恒定区。

29. 如权利要求17所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段包含IgA二聚体分子。

30. 如权利要求18所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段包含IgA二聚体分子。

31. 如权利要求19所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段包含IgA二聚体分子。

32. 如权利要求20所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段包含IgA二聚体分子。

33. 如权利要求21所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段包含IgA二聚体分子。

34. 如权利要求22所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段包含IgA二聚体分子。

35. 如权利要求17所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段包含分泌型IgA分子。

36. 如权利要求18所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段包含分泌型IgA分子。

37. 如权利要求19所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段包含分

泌型IgA分子。

38. 如权利要求20所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段包含分泌型IgA分子。

39. 如权利要求21所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段包含分泌型IgA分子。

40. 如权利要求22所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段包含分泌型IgA分子。

41. 如权利要求1所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段是单克隆的。

42. 如权利要求9所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段是单克隆的。

43. 如权利要求10所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段是单克隆的。

44. 如权利要求1所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段是嵌合的、人源化的或人的。

45. 如权利要求9所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段是嵌合的、人源化的或人的。

46. 如权利要求10所述的抗体或抗原结合片段,其中所述抗体或抗原结合片段是嵌合的、人源化的或人的。

47. 组合物,其包含权利要求1-46中任一项所述的抗体或抗原结合片段以及药学上可接受的载体、赋形剂或稀释剂。

48. 试剂盒,其包含:

(i) 第一抗体或其抗原结合片段,所述第一抗体或其抗原结合片段对弯曲杆菌鞭毛加帽蛋白(FliD)线性表位具有特异性;以及

(ii) 第二抗体或其抗原结合片段,所述第二抗体或其抗原结合片段对弯曲杆菌鞭毛加帽蛋白(FliD)构象表位具有特异性,其中:

(i) 所述第一抗体或抗原结合片段包含分别如SEQ ID NO: 9-14所示的HCDR1、HCDR2、HCDR3、LCDR1、LCDR2和LCDR3序列;以及

(ii) 所述第二抗体或抗原结合片段包含分别如SEQ ID NO: 25-30所示的HCDR1、HCDR2、HCDR3、LCDR1、LCDR2和LCDR3序列。

49. 如权利要求48所述的试剂盒,其中:

(i) 所述第一抗体或抗原结合片段包含与SEQ ID NO: 2具有至少85%的氨基酸同一性的VH以及与SEQ ID NO: 4具有至少85%的氨基酸同一性的VL;并且

(ii) 所述第二抗体或抗原结合片段包含与SEQ ID NO: 22具有至少85%的氨基酸同一性的VH以及与SEQ ID NO: 24具有至少85%的氨基酸同一性的VL。

50. 如权利要求49所述的试剂盒,其中:

(i) 所述第一抗体或抗原结合片段包含SEQ ID NO: 2所示的VH以及SEQ ID NO: 4所示的VK;并且

(ii) 所述第二抗体或抗原结合片段包含SEQ ID NO: 22所示的VH和SEQ ID NO: 24所

示的VL。

51. 如权利要求48所述的试剂盒,其中所述第一抗体或抗原结合片段以及所述第二抗体或抗原结合片段各自是相同的同种型。

52. 如权利要求51所述的试剂盒,其中所述第一抗体或抗原结合片段以及所述第二抗体或抗原结合片段各自是分泌型IgA。

53. 分离的多核苷酸,其编码权利要求1-46中任一项所述的抗体或抗原结合片段。

54. 如权利要求53所述的分离的多核苷酸,其中所述多核苷酸是密码子优化的,用于在宿主细胞中表达。

55. 如权利要求53或54所述的分离的多核苷酸,其包含:

(i) 编码VH的多核苷酸,其与SEQ ID NO:1、5、7、8、21、37或38中任一项所示的核苷酸序列具有至少75%的同一性;

(ii) 编码VL的多核苷酸,其与SEQ ID NO: 3、6、23或39所示核苷酸序列具有至少75%的同一性;和/或

(iii) 编码HCDR1、HCDR2、HCDR3、LCDR1、LCDR2和LCDR3的序列,其分别与SEQ ID NO: 15-20或分别与SEQ ID NO: 31-36所示的核苷酸序列具有至少90%的同一性。

56. 载体,其包含权利要求53-55中任一项所述的多核苷酸。

57. 重组宿主细胞,其包含权利要求53-55中任一项所述的分离的多核苷酸,或者权利要求56所述的载体。

58. 如权利要求57所述的重组宿主细胞,其中所述宿主细胞包含哺乳动物细胞。

59. 如权利要求58所述的重组宿主细胞,其中所述宿主细胞是CHO细胞、HEK293细胞、PER.C6细胞、Y0细胞、Sp2/0细胞、NS0细胞、人肝细胞、骨髓瘤细胞或杂交瘤细胞。

60. 制备权利要求1-46中任一项所述的抗体或抗原结合片段的方法,所述方法包括将权利要求57-59中任一项所述的重组宿主细胞在适于表达所述抗体或抗原结合片段的条件下和时间段培养。

61. 权利要求1-46中任一项所述的抗体或抗原结合片段或者权利要求47所述的组合物在制备用于治疗对象中的弯曲杆菌感染的药物中的用途。

62. 权利要求1-46中任一项所述的抗体或抗原结合片段或者权利要求47所述的组合物在制备用于减轻具有弯曲杆菌感染的对象中的肠道炎症的药物中的用途。

63. 权利要求1-46中任一项所述的抗体或抗原结合片段或者权利要求47所述的组合物在制备用于增加具有弯曲杆菌感染的对象中弯曲杆菌的肠道脱落的药物中的用途。

64. 如权利要求61-63中任一项所述的用途,其中所述抗体或抗原结合片段包含分泌型IgA分子。

65. 如权利要求61所述的用途,其中通过口服施用来施用所述抗体、抗原结合片段或组合物。

66. 如权利要求61所述的用途,其中向所述对象2次、3次、4次、5次、6次、7次、8次、9次、10次或更多次施用所述抗体、抗原结合片段或组合物。

67. 如权利要求61所述的用途,其中向所述对象多次施用所述抗体、抗原结合片段或组合物,其中在第一次施用或先前施用后6小时、7小时、8小时、9小时、10小时、11小时、12小时、24小时、48小时、74小时、96小时或更长时间分别进行第二次施用或逐次施用。

68. 如权利要求61所述的用途,其中在所述对象被所述弯曲杆菌感染之前向所述对象至少一次施用所述抗体、抗原结合片段或组合物。

69. 如权利要求61所述的用途,其中与施用有效量的所述抗体、抗原结合片段或组合物之前来自对象的粪便样品相比,在所述施用后来自所述对象的粪便样品包含增加数量的弯曲杆菌菌落形成单位(CFU)。

70. 如权利要求61所述的用途,其中与施用有效量的所述抗体、抗原结合片段或组合物之前来自对象的粪便样品相比,在所述施用后来自所述对象的粪便样品包含减少量的脂质运载蛋白-2(LCN2)。

71. 如权利要求61所述的用途,其中与施用有效量的所述抗体、抗原结合片段或组合物之前的对象相比,在所述施用后,所述对象包含在盲肠中减少量的多形核(PMN)细胞浸润,其中所述PMN细胞是Gr1⁺CD11b⁺。

72. 如权利要求61所述的用途,其中与施用有效量的所述抗体、抗原结合片段或组合物之前的对象相比,在所述施用后,所述对象具有改善的盲肠组织学。

73. 如权利要求61所述的用途,其中在所述施用后,所述抗体或抗原结合片段在所述施用后在所述对象的盲肠和/或排泄物中存在至少4小时或至少8小时。

74. 如权利要求1-46中任一项所述的抗体或抗原结合片段,或者如权利要求47所述的组合物,其用于以下的方法中:

- (a) 治疗对象中的弯曲杆菌感染;
- (b) 减轻具有弯曲杆菌感染的对象中的肠道炎症;和/或
- (c) 增加具有弯曲杆菌感染的对象中的弯曲杆菌的肠道脱落。

75. 如权利要求1-46中任一项所述的抗体或抗原结合片段,或者如权利要求47所述的组合物,其用于制造或制备药物的方法的用途中,所述药物用于:

- (a) 治疗对象中的弯曲杆菌感染;
- (b) 减轻具有弯曲杆菌感染的对象中的肠道炎症;和/或
- (c) 增加具有弯曲杆菌感染的对象中的弯曲杆菌的肠道脱落。

76. 如权利要求75所述用途的抗体或抗原结合片段或者组合物,其中所述药物被配制用于口服施用。

针对弯曲杆菌物种的抗体

[0001] 关于序列表的声明

[0002] 与本申请相关的序列表是以文本格式代替纸质副本提供的,并且在此通过引用并入本说明书中。包含序列表的文本文件的名称为470082_406WO_SEQUENCE_LISTING.txt。文本文件大小为304KB,在2019年7月16日创建,并通过EFS-Web以电子方式提交。

[0003] 背景

[0004] 弯曲杆菌是全世界细菌性肠胃炎的最常见原因,并且最近已经被添加到对人类健康造成潜在全球威胁的抗生素抗性细菌的世界卫生组织(WHO)列表中(参见,例如,“WHO publishes list of bacteria for which new antibiotics are urgently needed”, World Health Organization news release, 2017年2月27日; who.int/en/news-room/detail/27-02-2017-who-publishes-list-of-bacteria-for-which-new-antibiotics-are-urgently-needed)。弯曲杆菌物种((空肠弯曲杆菌(*Campylobacter jejuni*)和大肠弯曲杆菌(*Campylobacter coli*)))是发达国家旅行者腹泻的重要原因,并且是发展中国家2岁以下儿童危及生命的急性水样腹泻的主要原因。目前,还没有被批准用于预防弯曲杆菌病的疫苗。补液是治疗的主要形式,并且尽管已经显示抗生素在严重感染中是有益的,但通常不推荐抗生素以避免抗性的快速形成。

[0005] 因此,需要用于预防或治疗弯曲杆菌感染的新疗法。

[0006] 附图简述

[0007] 图1显示了与本公开内容的弯曲杆菌(“Campy”)反应性rSIgA的鼠微生物群的交叉反应性和宽度。

[0008] 图2显示了检查本公开内容的Campy反应性rSIgA限制细菌运动性的能力的细菌运动性测定的设计。

[0009] 图3显示了来自图2所示的实验的结果。培养板如下:(左至右) = 模拟感染;无mAb;对照rSIgA;Campy反应性rSIgA。

[0010] 图4A显示了C57BL/6小鼠粪便中的人IgA包被的细菌的FACS分析,所述小鼠在用 10^9 CFU的空肠弯曲杆菌菌株81-176感染之前1h接受预防剂量的Campy反应性rSIgA,然后在6h p.i.接受第二剂量的rSIgA。如所示,在4h、6h和9h p.i.取粪便样品。

[0011] 图4B显示了未感染(L)小鼠对比感染(R)小鼠的粪便中的抗HuIgA包被的细菌。

[0012] 图5A和5B显示了(A)感染后24小时和(B)感染后72小时处理的和未处理的动物中的弯曲杆菌脱落。

[0013] 图6显示了感染后24小时、48小时和72小时动物粪便中的脂质运载蛋白-2的ELISA定量。

[0014] 图7A-7E显示了与Flid结合的本公开内容的示例性抗体CAA1和CCG4(表达为rSIgA)的体外表征。(A)如通过ELISA测量的CAA1、CCG4和HGN194 rSIgA与包被的重组Flid的结合。将三种mAb的系列稀释液与Flid预包被的96孔ELISA板在室温下孵育1小时。使用生物素化的抗人类SC抗体,然后与链霉亲和素-AP孵育进行检测。(B)通过生物膜层干涉(BLI)进行的交叉竞争研究。将Flid抗原固定在APS传感器上,然后在与CCG4、CAA1或含有1%BSA

的PBS缔合之前与CAA1孵育。(C)在还原和变性条件下对CAA1、CCG4和HGN194rSIgA与Flid抗原(70KDa)结合的蛋白质印迹分析。(D)所示mAb对空肠弯曲杆菌和大肠弯曲杆菌的纯培养物的体外结合的代表性直方图。示出了三个中的一个代表性实验。(E)在共聚焦显微镜中观察到的CAA1、CCG4和HGN194 rSIgA2与空肠弯曲杆菌的结合。使用Syto BC对细菌进行染色,而使用缀合的抗人IgA AF647检测mAb。

[0015] 图8A-8D显示了C57BL/6刚断奶的小鼠对空肠弯曲杆菌感染高度敏感。(A-C)用 10^8 CFU的空肠弯曲杆菌口服感染12日龄、21日龄和56日龄的C57BL/6小鼠。(A)在感染后6天测定感染动物粪便中的细菌载量(CFU)和(B)脂质运载蛋白2(LCN2)。(C)来自感染小鼠的盲肠的代表性H&E切片和感染后6天的组织病理学评分的统计分析。白色箭头:粘膜下炎症;白色星号:隐窝增生以及杯状细胞数量减少;黑色星号:上皮脱屑;黑色箭头:粘膜炎症。比例尺:200 μ m。(D)在12日龄、21日龄和56日龄时C57BL/6小鼠中的排泄物IgA浓度的定量。点代表各小鼠,并且结果显示为 \pm SEM。使用曼-惠特尼(Mann-Whitney)检验(A-D)。 $*p<0.05$, $**p<0.01$ 。示出了两个中的一个代表性实验。

[0016] 图9A-9D显示了口服施用的CAA1和CCG4 rSIgA2对刚断奶小鼠中的空肠弯曲杆菌感染的预防活性。(A-D)在用 10^8 cfu的空肠弯曲杆菌感染之前两小时,用200 μ g在PBS中的指定mAb通过灌胃(gavage)口服给药21日龄的C57BL/6小鼠。(A)测定空肠弯曲杆菌感染后24h、48h和72h的排泄物细菌载量(CFU)。在不同的处理条件下,在感染后72h,测定(B)粪便中的脂质运载蛋白-2(LCN)水平,(C)以Gr1⁺CD11b⁺设门的多形核(PMN)细胞浸润的统计分析,以及(D)盲肠中的组织病理学评分。点代表各小鼠,并且结果显示为 \pm SEM。使用曼-惠特尼检验(A-D)。 $**p<0.05$, $**p<0.01$, $***p<0.001$ 。示出了至少两个中的一个代表性实验。

[0017] 图10A-10D显示了CAA1 SIgA1和SIgA2对空肠弯曲杆菌感染具有类似的预防活性。(A-D)在用 10^8 CFU的空肠弯曲杆菌感染之前两小时,用200 μ g的CAA1作为rSIgA1或rSIgA2通过灌胃口服给药21日龄的C57BL/6小鼠。(A)在感染后24h、48h和72h定量动物粪便中的细菌载量(CFU)。(B)在以Gr1⁺CD11b⁺设门的盲肠中浸润的多形核细胞的代表性点图和相对定量。在不同的处理条件下,在感染后72h,(C)粪便中的脂质运载蛋白-2(LCN)的定量,以及(D)盲肠中的组织病理学评分的统计分析。点代表各小鼠,并且结果显示为 \pm SEM。使用曼-惠特尼检验(A-D)。 $*p<0.05$, $**p<0.01$ 。示出了至少两个中的一个代表性实验。

[0018] 图11A-11D显示了转化为IgG降低了针对空肠弯曲杆菌感染的口服CAA1预防活性。(A-D)在用 10^8 CFU的空肠弯曲杆菌感染之前2h,用200 μ g的CAA1作为rSIgA2或rIgG1通过灌胃口服给药21日龄的C57BL/6小鼠。(A)在感染后24h、48h和72h定量动物粪便中的细菌载量(CFU)。(B)在以Gr1⁺CD11b⁺设门的盲肠中浸润的多形核细胞的代表性点图和相对定量。在不同的处理条件下,在感染后72h,(C)粪便中的脂质运载蛋白-2(LCN)的定量,以及(D)盲肠中的组织病理学评分的统计分析。点代表各小鼠,并且结果显示为 \pm SEM。使用曼-惠特尼检验(A-D)。 $*p<0.05$, $**p<0.01$ 。示出了至少两个中的一个代表性实验。

[0019] 图12显示了Flid氨基酸序列保守性的分析。从GenBank中检索来自空肠弯曲杆菌和大肠弯曲杆菌分离物的Flid氨基酸序列,并使用CLC Main Workbench软件(Qiagen)进行分析。序列标识图中每个字母的高度代表该氨基酸在特定位点的保守性水平。Flid的共有序列显示在顶部。

[0020] 图13显示了来自不同扁桃体样品的Flid反应性IgA⁺和IgG⁺记忆B细胞的频率。显示

了对不同扁桃体样品的IgA⁺ (上图)和IgG⁺ (下图)记忆B细胞库的Flid抗原的反应性的分析。

[0021] 图14A-14C显示了Flid反应性mAb与鼠微生物群的交叉反应性和在C57BL/6刚断奶小鼠的盲肠中的持久性。(A)所示的mAb对模拟感染有或感染有空肠弯曲杆菌或大肠弯曲杆菌的小鼠中排泄物微生物群的特异性结合的代表性直方图。示出了三个中的一个代表性实验。(B-C)通过在不同小鼠肠道子区室中的指定时间点HGN194 (B) rSIgA和 (C) rIgG抗体的ELISA的药代动力学评价。示出了至少两个中的一个代表性实验。

[0022] 图15A-15D提供了显示在不同空肠弯曲杆菌感染剂量下CAA1rSIgA的预防活性的进一步数据。(A-B)如在感染后24h、72h和120h用 10^7 或 10^9 CFU的空肠弯曲杆菌所测量的,用200 μ g CAA1 rSIgA2通过灌胃给药的21日龄的C57BL/6小鼠中的排泄物细菌载量(CFU)的定量。(C-D)如在用 10^7 或 10^9 CFU的空肠弯曲杆菌感染后120h所测量的,用200 μ g的CAA1 rSIgA2通过灌胃给药21日龄的C57BL/6小鼠中的排泄物脂质运载蛋白-2(LCN)的定量。点代表各小鼠,并且结果显示为 \pm SEM。使用曼-惠特尼检验(A-D)。* $p < 0.05$,** $p < 0.01$ 。示出了至少两个中的一个代表性实验。

[0023] 图16A-16D显示了IgA同种型转变影响IgAse敏感性,但不影响Flid亲和力或特异性。(A)用PBS或用来自淋病奈瑟球菌(*Neisseria gonorrhoeae*)的rIgA蛋白酶(IgAse Pro-Pro-Y-Pro)孵育过夜(18小时)的CAA1 rSIgA1和rSIgA2的变性非还原凝胶。(1:SIgA1+PBS; 2:SIgA2+PBS; 3:SIgA1+Igase; 4:SIgA2+Igase)。(B)如通过ELISA所测量的rSIgA1和rSIgA2 CAA1与Flid的结合。将mAb的系列稀释液与Flid预包被的96孔ELISA板在室温下孵育1小时。使用生物素化的抗人类SC抗体,然后与链霉亲和素-AP孵育进行检测。(C)所示的mAb对空肠弯曲杆菌和大肠弯曲杆菌的纯培养物的体外特异性结合的代表性直方图。示出了三个中的一个代表性实验。(D)CAA1 rSIgA1和rSIgA2与未感染的C57BL/6刚断奶的小鼠的排泄物微生物群结合的代表性直方图。

[0024] 图17A-17D显示了转化为IgG形式降低了针对空肠弯曲杆菌感染的口服CCG4预防活性。(A-D)在用 10^8 CFU的空肠弯曲杆菌感染之前2h,用200 μ g CCG4作为rSIgA2或rIgG1通过灌胃口服给药21日龄的C57BL/6小鼠。(A)在感染后24h和72h动物粪便中的细菌载量(CFU)的定量。(B)在感染后72h在盲肠中浸润的多形核细胞的代表性点图和相对定量。在不同的处理条件下,在感染后72h, (C)粪便中的脂质运载蛋白-2(LCN)的定量,以及(D)盲肠中的组织病理学评分的统计分析。点代表各小鼠,并且结果显示为 \pm SEM。使用曼-惠特尼检验(A-D)。* $p < 0.05$,** $p < 0.01$ 。示出了两个中的一个代表性实验。

[0025] 详述

[0026] 本文提供了对弯曲杆菌具有特异性的抗体和抗原结合片段,包含其的组合物,以及使用所述抗体和组合物治疗(例如,减少、延迟、消除或预防)对象中的弯曲杆菌感染的方法。在一些实施方案中,本公开内容的抗体包含IgA分子,例如二聚IgA分子。在某些实施方案中,如本文所述,本公开内容的IgA抗体以分泌形式(SIgA)提供。施用本公开内容的抗体和抗原结合片段,例如,通过口服递送本公开内容的SIgA,可以治疗弯曲杆菌(例如与严重的新生儿肠胃炎相关的弯曲杆菌物种)感染。

[0027] 作为背景,弯曲杆菌是全世界腹泻的确定原因,并且最近已经被添加到对人类健康造成全球威胁的抗生素抗性细菌的WHO列表中(世界卫生组织(WHO),2017)。弯曲杆菌的流行病学在高收入国家和中低收入国家之间不同,在高收入国家中,遇到这种细菌是偶发

的,而在中低收入国家中,感染在儿童早期几乎是普遍的,并且是婴幼儿中威胁生命的急性水样腹泻的主要原因(Riddle和Guerry,Vaccine,34:2903-2906(2016))。

[0028] 弯曲杆菌感染被认为是一种主要的人畜共患病,主要与食用受污染的未煮熟的动物肉(家禽是主要的细菌库)、水或未经巴氏消毒的奶有关(Kaakoush等人,Clin.Microbiol.Rev.,28:687-720(2015))。空肠弯曲杆菌和大肠弯曲杆菌是人类中弯曲杆菌肠炎的主要原因(Man,Nat.Rev.Gastroenterol.Hepatol.,8:669-685(2011))。

[0029] 弯曲杆菌病通常导致以水样或血性腹泻、发热、体重减轻和平均持续6天的痉挛为特征的急性胃肠疾病(Kaakoush等人,Clin.Microbiol.Rev.,28:687-720(2015);世界卫生组织(WHO)(2013))。与弯曲杆菌肠炎有关的严重脱水是新生儿和儿童,特别是发展中国家中死亡的重要原因(Platts-Mills等人,Lancet Glob.Health.,3:e564-75(2015))。此外,空肠弯曲杆菌感染一直与自身免疫病况例如格林-巴利综合征(Guillain-Barré Syndrome, GBS)(Islam等人,PLoS One,7:e43976(2012);Yuki等人,Proc.Natl.Acad.Sci.U.S.A.,101:11404-11409(2004))和炎症性肠病(IBD)(Gradel等人,Gastroenterology,137:495-501(2009))的发作有关。

[0030] 如实验动物模型和人类健康志愿者研究中所示,认为鞭毛介导的运动性对于弯曲杆菌的毒力和致病性是重要的(Black等人,J.Infect.Dis.,157:472-479(1988);Morooka等人,J.Gen.Microbiol.,131:1973-1980(1985))。但是,鞭毛蛋白(FlaA),即鞭毛的主要成分,即使在相同的空肠弯曲杆菌物种中也不存在高水平的保守性,并且它的巨大的糖基化模式根据菌株和生长阶段而变化很大(Parkhill等人,Nature,403:665-668(2000);Thibault等人,J.Biol.Chem.,276:34862-34870(2001))。空肠弯曲杆菌鞭毛蛋白的重组非糖基化形式在临床试验中显示出差的免疫原性(Riddle和Guerry,Vaccine,34:2903-2906(2016)),使得FlaA成为治疗的挑战性靶标。此外,在疫苗中使用空肠弯曲杆菌的可能性受到与细菌脂寡糖(LOS)的神经节苷脂模拟相关的GBS发展的风险的限制(Riddle和Guerry,Vaccine,34:2903-2906(2016))。

[0031] 由于这些缺点,目前尚无全球管理机构批准的预防弯曲杆菌感染的疫苗。补液是治疗的主要形式,尽管已经显示抗生素在严重感染中是有益的,但由于抗生素抗性的快速形成,因此通常不推荐抗生素。即使在从感染中恢复的情况下,低收入国家的婴幼儿持续暴露于肠道病原体(包括弯曲杆菌)也已经与环境肠病(EE)/环境肠道功能障碍(EED)(与营养素吸收不良有关的小肠的亚临床慢性炎症)、生长缓慢、认知发展受损、微生物群的变化和对口服疫苗接种的反应性降低有关(Watanabe和Petri,EBioMedicine,10:25-32(2016))。

[0032] 本公开内容提供了结合弯曲杆菌鞭毛加帽蛋白FlhD的抗体和抗原结合片段。根据本公开内容的抗体有利地限制了弯曲杆菌的运动性,并且在本公开内容所述的弯曲杆菌感染的动物模型中,能够加强弯曲杆菌清除感染,显著降低与上皮损伤和多形核(PMN)细胞浸润有关的炎症标志物的水平。

[0033] 本文还提供了包含本公开内容的弯曲杆菌FlhD特异性抗体或抗原结合片段的组合物,编码所述抗体或抗原结合片段的多核苷酸,包含所述多核苷酸的载体以及表达所述抗体或抗原结合片段和/或包含或含有本公开内容的多核苷酸或载体的宿主细胞。还提供了用于治疗弯曲杆菌感染和/或用于减轻相关症状的方法和用途。

[0034] 还提供了用于研究弯曲杆菌感染的非人动物模型。

[0035] 在更详细地阐述本公开内容之前,提供本文所用的某些术语的定义可能有助于理解本公开内容。在整个本公开内容中阐述了另外的定义。

[0036] 在本说明书中,除非另有说明,否则任何浓度范围、百分比范围、比率范围或整数范围应理解为包括所述范围内的任何整数的值,以及在适当时包括其分数(例如整数的十分之一和百分之一)。另外,除非另有说明,否则本文所述的与任何物理特征相关的任何数值范围,例如聚合物亚单位、尺寸或厚度,应理解为包括所述范围内的任何整数。如本文所用,除非另有说明,否则术语“约”意指所示范围、值或结构的 $\pm 20\%$ 。应理解,如本文所用的术语“一个/一种(a)”和“一个/一种(an)”是指所列举组分中的“一个或多个/一种或多种”。替代方案(例如,“或”)的使用应理解为意指替代方案中的一个、两个或其任何组合。如本文所用,术语“包括(include)”、“具有(have)”和“包含(comprise)”是同义使用的,这些术语及其变体旨在解释为非限制性的。

[0037] “任选的”或“任选地”意指随后描述的要素、组分、事件或情况可以发生或可以不发生,并且该描述包括要素、组分、事件或情况发生的情况和它们不发生的情况。

[0038] 此外,应理解,本申请公开了衍生自本文所述结构和亚单位的各种组合的单独构建体或构建体组,其程度如同每个构建体或构建体组单独阐述一样。因此,特定结构或特定亚单元的选择在本公开内容的范围内。

[0039] 术语“基本上由……组成”不等同于“包含”,并且是指权利要求书的指定材料或步骤,或者是指不会实质上影响所要求保护的主题的基本特征的那些。例如,蛋白质结构域、区或模块(例如,结合结构域、铰链区或接头)或蛋白质(其可以具有一个或多个结构域、区或模块)基本上由当结构域、区、模块或蛋白质的氨基酸序列包括组合构成结构域、区、模块或蛋白质的长度的至多20%(例如,至多15%、10%、8%、6%、5%、4%、3%、2%或1%)并且基本上不影响(即,活性降低不超过50%,例如不超过40%、30%、25%、20%、15%、10%、5%或1%)结构域、区、模块或蛋白质的活性(例如,结合蛋白的靶标结合亲和力)的延伸、缺失、突变或其组合(例如,氨基末端或羧基末端处或者结构域之间的氨基酸)时的特定氨基酸序列组成。

[0040] 如本文所用,“氨基酸”是指天然存在的氨基酸和合成的氨基酸,以及氨基酸类似物和氨基酸模拟物,其以类似于天然存在的氨基酸的方式起作用。天然存在的氨基酸是由遗传密码编码的那些氨基酸以及后来被修饰的那些氨基酸,例如羟脯氨酸、 γ -羧基谷氨酸和0-磷酸丝氨酸。氨基酸类似物是指具有与天然存在的氨基酸相同的基本化学结构的化合物,即,与氢、羧基、氨基和R基团结合的 α -碳,例如,高丝氨酸、正亮氨酸、甲硫氨酸亚砷、甲硫氨酸甲基砷。此类类似物具有修饰的R基团(例如正亮氨酸)或修饰的肽骨架,但保留与天然存在的氨基酸相同的基本化学结构。氨基酸模拟物是指具有与氨基酸的一般化学结构不同的结构,但以类似于天然存在的氨基酸的方式起作用的化学化合物。

[0041] 如本文所用,“突变”是指分别与参照或野生型核酸分子或多肽分子相比核酸分子或多肽分子的序列的变化。突变可以导致几种不同类型的序列变化,包括核苷酸或氨基酸的取代、插入或缺失。

[0042] “保守取代”是指不显著影响或改变特定蛋白质的结合特性的氨基酸取代。通常,保守取代是其中取代的氨基酸残基被具有类似侧链的氨基酸残基取代的取代。保守取代包括在以下组之一中发现的取代:第1组:丙氨酸(Ala或A)、甘氨酸(Gly或G)、丝氨酸(Ser或

S)、苏氨酸(Thr或T);第2组:天冬氨酸(Asp或D)、谷氨酸(Glu或Z);第3组:天冬酰胺(Asn或N)、谷氨酰胺(Gln或Q);第4组:精氨酸(Arg或R)、赖氨酸(Lys或K)、组氨酸(His或H);第5组:异亮氨酸(Ile或I)、亮氨酸(Leu或L)、甲硫氨酸(Met或M)、缬氨酸(Val或V);和第6组:苯丙氨酸(Phe或F)、酪氨酸(Tyr或Y)、色氨酸(Trp或W)。另外地或可选地,可以通过类似的功能、化学结构或组成(例如酸性、碱性、脂肪族、芳香族或含硫的)将氨基酸分组为保守取代基团。例如,出于取代的目的,脂肪族基团可以包括Gly、Ala、Val、Leu和Ile。其它保守取代基团包括:含硫的:Met和半胱氨酸(Cys或C);酸性:Asp、Glu、Asn和Gln;小的脂肪族的非极性或略有极性的残基:Ala、Ser、Thr、Pro和Gly;极性的带负电荷的残基及其酰胺:Asp、Asn、Glu和Gln;极性的带正电荷的残基:His、Arg和Lys;大的脂肪族的非极性残基:Met、Leu、Ile、Val和Cys;和大的芳香族残基:Phe、Tyr和Trp。另外的信息可以见于Creighton (1984) *Proteins*, W.H. Freeman and Company。

[0043] 如本文所用,“蛋白质”或“多肽”是指氨基酸残基的聚合物。蛋白质适用于天然存在的氨基酸聚合物,以及其中一个或多个氨基酸残基是相应的天然存在的氨基酸和非天然存在的氨基酸聚合物的人工化学模拟物的氨基酸聚合物。也考虑了本公开内容的蛋白质、肽和多肽的变体。在某些实施方案中,变体蛋白、肽和多肽包含与本文所述的限定的或参照的氨基酸序列的氨基酸序列至少70%、75%、80%、85%、90%、91%、92%、93%、94%、95%、96%、97%、98%、99%或99.9%相同的氨基酸序列或者由其组成。

[0044] “核酸分子”或“多核苷酸”或“多核酸”是指包括共价连接的核苷酸的聚合化合物,其可以由天然亚单位(例如,嘌呤或嘧啶碱基)或非天然亚单位(例如,吗啉环)组成。嘌呤碱基包括腺嘌呤、鸟嘌呤、次黄嘌呤和黄嘌呤、嘧啶碱基包括尿嘧啶、胸腺嘧啶和胞嘧啶。核酸分子包括多核糖核酸(RNA),其包括mRNA、微RNA、siRNA、病毒基因组RNA和合成RNA;以及多脱氧核糖核酸(DNA),其包括cDNA、基因组DNA和合成DNA,它们中的任一种可以是单链的或双链的。如果是单链的,则核酸分子可以是编码链或非编码(反义)链。编码氨基酸序列的核酸分子包括编码相同氨基酸序列的所有核苷酸序列。核苷酸序列的一些形式也可以包括达到这样的程度的内含子:可以通过共转录机制或转录后机制去除内含子。换句话说,由于遗传密码的冗余性或简并性或者通过剪接,不同的核苷酸序列可以编码相同的氨基酸序列。

[0045] 还考虑了本公开内容的核酸分子的变体。变体核酸分子是与如本文所述的限定的或参照的多核苷酸至少70%、75%、80%、85%、90%,并且优选95%、96%、97%、98%、99%或99.9%相同的核酸分子,或者在约65-68°C下在0.015M氯化钠、0.0015M柠檬酸钠或者在约42°C下在0.015M氯化钠、0.0015M柠檬酸钠和50%甲酰胺的严格杂交条件下与多核苷酸杂交。核酸分子变体保留了编码其结合结构域的能力,所述结合结构域具有本文所述的功能,例如结合靶标分子。

[0046] “序列同一性百分比”是指如通过比较序列所确定的两个或更多个序列之间的关系。确定序列同一性的优选方法被设计为给出被比较的序列之间的最佳匹配。例如,为了最佳的比较目的对序列进行比对(例如,为了最佳的比对,可以在第一和第二氨基酸或核酸序列中的一个或两个中引入缺口)。此外,为了比较的目的,可以忽略非同源序列。除非另有说明,否则本文提及的序列同一性百分比是在参照序列的长度上计算的。确定序列同一性和相似性的方法可以在公开获得的计算机程序中找到。可以使用BLAST程序(例如,BLAST 2.0、BLASTP、BLASTN或BLASTX)进行序列比对和同一性百分比计算。在BLAST程序中使用的

数学算法可以在Altschul等人,Nucleic Acids Res.25:3389-3402,1997中找到。在本公开内容的上下文中,将理解,在使用序列分析软件进行分析的情况下,分析的结果是基于所引用程序的“默认值”。“默认值”意指当第一次初始化时最初用软件加载的任一组数值或参数。

[0047] 术语“分离的”意指将材料从其原始环境(例如,如果是天然存在的,则为天然环境中)中移除。例如,不分离存在于活体动物中的天然存在的核酸或多肽,而是分离与天然系统中的一些或全部共存材料分离的相同核酸或多肽。此类核酸可以是载体的一部分和/或此类核酸或多肽可以是组合物(例如细胞裂解物)的一部分,并且仍然被分离,因为此类载体或组合物不是核酸或多肽的天然环境的一部分。

[0048] 术语“基因”意指参与产生多肽链的DNA或RNA的区段;它包括在编码区之前和之后的区域(例如,5'非翻译区(UTR)和3'UTR)以及在各个编码区段(外显子)之间的插入序列(内含子)。

[0049] “功能变体”是指这样的多肽或多核苷酸,其在结构上类似于或在结构上基本类似于本公开内容的母体化合物或参照化合物,但在组成上略有不同(例如,一个碱基、原子或官能团是不同的,添加或去除一个碱基、原子或官能团),使得所述多肽或编码的多肽能够以至少50%的效率,优选亲本多肽活性的至少55%、60%、70%、75%、80%、85%、90%、95%、96%、97%、98%、99%、99.9%或100%的水平来执行亲本多肽的至少一种功能。换句话说,与亲本多肽或参照多肽相比,当功能变体在选定的测定,例如用于测量结合亲和力的测定(测量缔合(Ka)或解离(KD)常数的Biacore®或四聚体染色)中显示出不超过50%的性能降低时,本公开内容的多肽或编码的多肽具有“类似的结合”、“类似的亲和力”或“类似的活性”。

[0050] 如本文所用,“功能部分”或“功能片段”是指仅包含母体化合物或参照化合物的结构域、部分或片段的多肽或多核苷酸,并且所述多肽或编码的多肽保留了与母体化合物或参照化合物的结构域、部分或片段相关的至少50%的活性,优选亲本多肽活性的至少55%、60%、70%、75%、80%、85%、90%、95%、96%、97%、98%、99%、99.9%或100%的水平,或者提供了生物益处(例如效应子功能)。当与亲本多肽或参照多肽相比时,当功能部分或片段在选定的测定中显示出不超过50%的性能降低时,本公开内容的多肽或编码的多肽的“功能部分”或“功能片段”具有“类似的结合”或“类似的活性”(对于亲和力,与亲本或参照相比,优选不超过20%或10%,或者不超过对数差)。

[0051] 如本文所用,术语“工程改造的”、“重组的”或“非天然的”是指包括至少一种遗传改变或已通过引入外源或异源核酸分子修饰的有机体、微生物、细胞、核酸分子或载体,其中所述改变或修饰通过遗传工程(即,人为干预)引入。遗传改变包括,例如,引入编码功能性RNA、蛋白质、融合蛋白或酶的可表达核酸分子的修饰,或者细胞遗传物质的其它核酸分子添加、缺失、取代或其它功能破坏。另外的修饰包括,例如,非编码调节区,其中修饰改变多核苷酸、基因或操纵子的表达。

[0052] 如本文所用,“异源的”或“非内源的”或“外源的”是指对于宿主细胞或对象不是天然的任何基因、蛋白质、化合物、核酸分子或活性,或者对于已经改变的宿主细胞或对象是天然的任何基因、蛋白质、化合物、核酸分子或活性。异源的、非内源的或外源的包括已经被突变或以其它方式改变,使得结构、活性或两者在天然的和改变的基因、蛋白质、化合物或

核酸分子之间是不同的基因、蛋白质、化合物或核酸分子。在某些实施方案中,异源的、非内源的或外源的基因、蛋白质或核酸分子(例如受体、配体等)可以不是宿主细胞或对象内源的,而是可以通过缀合、转化、转染、电穿孔等将编码此类基因、蛋白质或核酸分子的核酸添加到宿主细胞中,其中添加的核酸分子可以整合到宿主细胞基因组中或者可以作为染色体外遗传物质(例如,作为质粒或其它自我复制载体)存在。术语“同源的”或“同源物”是指在宿主细胞、物种或菌株中发现的或衍生自宿主细胞、物种或菌株的基因、蛋白质、化合物、核酸分子或活性。例如,编码多肽的异源或外源的多核苷酸或基因可以与天然多核苷酸或基因同源并编码同源多肽或活性,但多核苷酸或多肽可以具有改变的结构、序列、表达水平或其任意组合。非内源的多核苷酸或基因以及编码的多肽或活性可以来自相同的物种、不同的物种或其组合。

[0053] 在某些实施方案中,如果宿主细胞天然的核酸分子或其部分已经被改变或突变,则认为它是宿主细胞异源的,或者如果宿主细胞天然的核酸分子已经被异源表达控制序列改变或已经被通常与宿主细胞天然的核酸分子不相关的内源表达控制序列改变,则认为它是异源的。此外,术语“异源的”可以指与宿主细胞不同的,宿主细胞改变的或不是宿主细胞内源的生物活性。如本文所述,可以将一个以上的异源核酸分子作为单独的核酸分子、作为多个单独控制的基因、作为多顺反子核酸分子、作为编码融合蛋白的单个核酸分子或其任意组合引入宿主细胞。

[0054] 如本文所用,术语“内源的”或“天然的”是指通常存在于宿主细胞或对象中的多核苷酸、基因、蛋白质、化合物、分子或活性。

[0055] 本文所用的术语“表达”是指基于核酸分子例如基因的编码序列产生多肽的过程。该过程可以包括转录、转录后控制、转录后修饰、翻译、翻译后控制、翻译后修饰或其任何组合。表达的核酸分子通常与表达控制序列(例如启动子)可操作地连接。

[0056] 术语“可操作地连接”是指在单个核酸片段上两个或更多个核酸分子的缔合,使得一个核酸分子的功能受到另一个核酸分子的影响。例如,当启动子能够影响编码序列的表达时(即,编码序列处于启动子的转录控制之下),启动子与编码序列可操作地连接。“未连接的”意指相关的遗传元件彼此不紧密相关,并且一个的功能不影响另一个。

[0057] 如本文所述,可以将一个以上的异源核酸分子作为单独的核酸分子、作为多个单独控制的基因、作为多顺反子核酸分子、作为编码融合蛋白的单个核酸分子或其任意组合引入宿主细胞。当将两个或更多个异源核酸分子引入宿主细胞时,应理解,可以将两个或更多个异源核酸分子作为单个核酸分子(例如,在单个载体上)、在分开的载体上、在单个位点或多个位点整合到宿主染色体中、或其任何组合引入。所提及的异源核酸分子或蛋白质活性的数量是指编码核酸分子的数量或蛋白质活性的数量,而不是引入宿主细胞的单独核酸分子的数量。

[0058] 术语“构建体”是指含有重组核酸分子的任何多核苷酸(或者,当上下文清楚地指明时,本公开内容的融合蛋白)。(多核苷酸)构建体可以存在于载体(例如,细菌载体、病毒载体)中或可以整合到基因组中。“载体”是能够转运另一种核酸分子的核酸分子。载体可以是,例如,质粒、粘粒、病毒、RNA载体或者线性或环状DNA或RNA分子,其可以包括染色体、非染色体、半合成或合成的核酸分子。本公开内容的载体还包括转座子系统(例如,睡美人,参见,例如,Geurts等人,Mol. Ther. 8:108,2003;Mátés等人,Nat. Genet. 41:753,2009)。示例

性载体是能够自主复制(附加型载体),能够将多核苷酸递送到细胞基因组(例如病毒载体),或者能够表达与其连接的核酸分子(表达载体)的那些载体。

[0059] 如本文所用,“表达载体”或“载体”是指含有核酸分子的DNA构建体,所述核酸分子与能够在合适的宿主中实现核酸分子表达的合适控制序列可操作地连接。此类控制序列包括实现转录的启动子、控制此类转录的任意的操纵子序列、编码合适的mRNA核糖体结合位点的序列以及控制转录和翻译终止的序列。载体可以是质粒、噬菌体颗粒、病毒或仅仅是潜在基因组插入物。一旦转化到合适的宿主中,载体可以独立于宿主基因组复制和发挥功能,或者在一些情况下,可以整合到基因组本身中或将载体中包含的多核苷酸递送到没有载体序列的基因组中。在本说明书中,“质粒”、“表达质粒”、“病毒”和“载体”通常可互换使用。

[0060] 在将核酸分子插入细胞的上下文中,术语“引入的”意指“转染”、“转化”或“转导”,并且包括提及将核酸分子掺入真核细胞或原核细胞中,其中所述核酸分子可以掺入到细胞的基因组(例如,染色体、质粒、质体或线粒体DNA)中,转化为自主复制子或瞬时表达(例如转染的mRNA)。

[0061] 在某些实施方案中,本公开内容的多核苷酸可以与载体的某些元件可操作地连接。例如,可以可操作地连接多核苷酸序列,其是实现其所连接的编码序列的表达和加工所需的。表达控制序列可以包括适当的转录起始、终止、启动子和增强子序列;有效的RNA处理信号,如剪接和聚腺苷酸化信号;稳定细胞质mRNA的序列;增强翻译效率的序列(即Kozak共有序列);增强蛋白质稳定性的序列;以及可能增强蛋白质分泌的序列。如果表达控制序列与目的基因邻接,则该表达控制序列可以可操作地连接,所述表达控制序列以反式起作用或在一定距离起作用以控制目的基因。

[0062] 在某些实施方案中,载体包含质粒载体或病毒载体(例如,慢病毒载体或 γ -逆转录病毒载体)。病毒载体包括逆转录病毒,腺病毒,细小病毒(例如腺相关病毒),冠状病毒,负链RNA病毒如正粘病毒(例如流感病毒),弹状病毒(例如狂犬病病毒和水疱性口炎病毒),副粘病毒(例如麻疹和仙台病毒),正链RNA病毒如小核糖核酸病毒和甲病毒,以及双链DNA病毒,包括腺病毒,疱疹病毒(例如,单纯疱疹病毒1型和2型、Epstein-Barr病毒、巨细胞病毒)和痘病毒(例如,痘苗、禽痘和金丝雀痘)。其它病毒包括,例如诺沃克病毒、披膜病毒、黄病毒、呼肠孤病毒、乳多空病毒、嗜肝DNA病毒和肝炎病毒。逆转录病毒的实例包括禽类白血病-肉瘤,哺乳动物C-型病毒、B-型病毒、D型病毒,HTLV-BLV组病毒,慢病毒,泡沫病毒(Coffin, J.M., *Retroviridae: The viruses and their replication*, In *Fundamental Virology*, 第三版, B.N. Fields等人编辑, Lippincott-Raven Publishers, Philadelphia, 1996)。

[0063] “逆转录病毒”是具有RNA基因组的病毒,其使用逆转录酶将所述RNA基因组逆转录成DNA,然后将逆转录的DNA掺入到宿主细胞基因组中。“ γ 逆转录病毒”是指逆转录病毒科的一个属。 γ 逆转录病毒的实例包括小鼠干细胞病毒、小鼠白血病病毒、猫白血病病毒、猫肉瘤病毒和禽网状内皮增生症病毒。

[0064] “慢病毒载体”包括用于基因递送的基于HIV的慢病毒载体,其可以是整合的或非整合的,具有相对大的包装能力,并且可以转导一系列不同的细胞类型。慢病毒载体通常在三种(包装、包膜和转移)或更多种质粒瞬时转染到生产细胞后产生。像HIV一样,慢病毒载体通过病毒表面糖蛋白与细胞表面上受体的相互作用进入靶细胞。在进入时,病毒RNA经历

由病毒逆转录酶复合物介导的逆转录。逆转录产物是双链线性病毒DNA,其是病毒整合到感染细胞的DNA中的底物。

[0065] 在某些实施方案中,病毒载体可以是 γ 逆转录病毒,例如莫洛尼鼠白血病病毒(MLV)衍生的载体。在其它实施方案中,病毒载体可以是更复杂的逆转录病毒衍生的载体,例如慢病毒衍生的载体。HIV-1衍生的载体属于这一类别。其它实例包括衍生自HIV-2、FIV、马传染性贫血病毒、SIV和Maedi-Visna病毒(绵羊慢病毒)的慢病毒载体。使用逆转录病毒和慢病毒病毒载体以及包装细胞用于利用含有转基因的病毒颗粒转导哺乳动物宿主细胞的方法是本领域已知的,并且先前已描述于例如美国专利8,119,772;Walchli等人,PLoS One 6:327930,2011;Zhao等人,J.Immunol.174:4415,2005;Engels等人,Hum.Gene Ther.14:1155,2003;Frecha等人,Mol.Ther.18:1748,2010;以及Verhoeyen等人,Methods Mol.Biol.506:97,2009。逆转录病毒和慢病毒载体构建体和表达系统也是可商购获得的。其它病毒载体也可用于多核苷酸递送,包括DNA病毒载体,包括例如基于腺病毒的载体和基于腺相关病毒(AAV)的载体;衍生自单纯疱疹病毒(HSV)的载体,包括扩增子载体,复制缺陷型HSV和减毒的HSV(Kriskey等人,Gene Ther.5:1517,1998)。

[0066] 可用于本公开内容的组合物和方法的其它载体包括衍生自杆状病毒和 α -病毒的那些载体(Jolly,D J.1999.Emerging Viral Vectors.pp209-40in Friedmann T.ed.The Development of Human Gene Therapy.New York:Cold Spring Harbor Lab)或质粒载体(例如睡美人或其它转座子载体)。

[0067] 当病毒载体基因组包含将在宿主细胞中作为单独的转录物表达的多个多核苷酸时,病毒载体还可以在两个(或更多个)转录物之间包含另外的序列,允许双顺反子或多顺反子表达。病毒载体中使用的此类序列的实例包括内部核糖体进入位点(IRES)、弗林蛋白酶切割位点、病毒2A肽或其任何组合。

[0068] 如本文所用,术语“宿主”是指靶向用异源核酸分子进行遗传修饰以产生目的多肽(例如,本公开内容的抗体)的细胞或微生物。

[0069] 宿主细胞可以包括任何单独的细胞或细胞培养物,其可以接受载体或核酸的掺入或表达蛋白质。该术语还涵盖宿主细胞的后代,无论是遗传上还是表型上相同或不同。合适的宿主细胞可以取决于载体,并且可以包括哺乳动物细胞、动物细胞、人细胞、猿细胞、昆虫细胞、酵母细胞和细菌细胞。可以通过使用病毒载体,通过磷酸钙沉淀,DEAE-葡聚糖,电穿孔,显微注射或其它方法的转化来诱导这些细胞掺入载体或其它材料。参见,例如,Sambrook等人,Molecular Cloning:A Laboratory Manual 2d ed.(Cold Spring Harbor Laboratory,1989)。

[0070] 如本文所用,“鞭毛加帽蛋白”,也称为“FliD”和“钩相关蛋白2(HAP2)”,是在空肠弯曲杆菌和大肠弯曲杆菌物种中具有高的序列保守性的一种约70kDa的蛋白(Chintoan-Uta等人,Vaccine,34:1739-1743(2016)) (例如,图12;SEQ ID NO:43-95)。不希望受理论的束缚,认为弯曲杆菌FliD寡聚物形成位于鞭毛尖端的帽蛋白复合物,其通过调节鞭毛蛋白分子的组装来控制细丝的远端生长。由于其在细丝伸长中的功能作用,FliD缺陷型突变体在细菌运动性中表现出缺陷(Song等人,J.Mol.Biol.,429:847-857(2017))。已经提出FliD参与细胞粘附(Freitag等人,Cell.Microbiol.,(2017))和鸡在自然感染期间的免疫原性。

[0071] 本文所用的“抗原”或“Ag”是指引起免疫应答的免疫原性分子。这种免疫应答可涉

及抗体产生、特异性免疫活性细胞的活化、补体的活化、抗体依赖性细胞毒性或其任何组合。抗原(免疫原性分子)可以是,例如,肽、糖肽、多肽、糖多肽、多核苷酸、多糖、脂质等。很明显,抗原可以被合成、重组产生或衍生自生物样品。可以含有一种或多种抗原的示例性生物样品包括组织样品、粪便样品、细胞、生物流体或其组合。抗原可以由经过修饰或基因工程改造以表达抗原的细胞产生。抗原也可以存在于弯曲杆菌中;例如,FliD蛋白或其部分。

[0072] 术语“表位”或“抗原表位”包括被同源结合分子识别和特异性结合的任何分子、结构、氨基酸序列或蛋白决定簇,所述同源结合分子例如免疫球蛋白或其它结合分子、结构域或蛋白。表位决定簇通常包含分子的化学活性表面基团,例如氨基酸或糖侧链,并且可以具有特定的三维结构特征以及特定的电荷特征。当抗原是或包含肽或蛋白质时,表位可以包含连续的氨基酸(例如,线性表位);或者可以包含来自蛋白质的不同部分或区域的氨基酸,所述蛋白质的不同部分或区域通过蛋白质折叠(例如,不连续或构象表位)而接近;或者与蛋白质折叠无关地紧密接近的非连续氨基酸。

[0073] 抗体、抗原结合片段和组合物

[0074] 在一个方面,本公开内容提供了分离的抗体或其抗原结合片段,所述抗体或其抗原结合片段对弯曲杆菌鞭毛加帽蛋白(FliD)表位具有特异性。在某些实施方案中,表位是构象表位。在其它实施方案中,表位是线性表位。

[0075] 本公开内容的抗体或抗原结合片段对于FliD表位或抗原具有“特异性”,意味着它与表位或包含表位的抗原缔合或结合,而不与样品中的任何其它分子或组分显著缔合或结合。在某些实施方案中,本公开内容的抗体或抗原结合片段与FliD缔合或结合(unite)(例如,结合(bind)),而不与样品中存在的其它分子或组分(例如,其它抗原或潜在抗原,包括其它弯曲杆菌蛋白)显著缔合或结合。在某些实施方案中,本公开内容的对FliD具有特异性的抗体或抗原结合片段能够以如通过ELISA测量的小于约0.1 $\mu\text{g}/\text{mL}$,或小于约0.05 $\mu\text{g}/\text{mL}$,或小于约0.03 $\mu\text{g}/\text{mL}$ 的EC50结合FliD表位。在某些实施方案中,抗体或抗原结合片段能够以约0.03 $\mu\text{g}/\text{mL}$ 、或约0.025 $\mu\text{g}/\text{mL}$ 、或约0.020 $\mu\text{g}/\text{mL}$ 的EC50结合FliD表位。

[0076] 在某些实施方案中,本公开内容的抗体或抗原结合片段能够以如通过ELISA(例如,利用OD450nm的读数)测量的小于约0.1 $\mu\text{g}/\text{mL}$ (即,小于约0.1、0.09、0.08、0.07、0.06、0.05、0.04、0.03、0.025或0.02 $\mu\text{g}/\text{mL}$,或更小)的EC50结合FliD表位。在某些实施方案中,本公开内容的抗体或抗原结合片段能够以如通过ELISA(例如,用OD450nm的读数)测量的小于约0.05 $\mu\text{g}/\text{mL}$ 或小于约0.03 $\mu\text{g}/\text{mL}$ 的EC50结合FliD表位。

[0077] 用于测量针对FliD的抗体或抗原结合片段的EC50的示例性测定包括将抗体或抗原结合片段与FliD预包被的96孔ELISA板在室温下孵育约1h,然后使用生物素化的抗Ig SC抗体,然后与链霉亲和素-AP孵育进行检测。

[0078] 如本文所用,“特异性结合”是指抗体或抗原结合片段以等于或大于 10^5M^{-1} (其等于该缔合反应的结合速率 $[K_{\text{on}}]$ 与解离速率 $[K_{\text{off}}]$ 的比率)的亲合力或 K_a (即,以1/M为单位的特定结合相互作用的平衡缔合常数)与抗原的缔合或结合,而不与样品中的任何其它分子或组分显著缔合或结合。可选地,亲合力可以被定义为以M为单位的特定结合相互作用的平衡解离常数(K_d)(例如, 10^{-5}M 至 10^{-13}M)。抗体可以被分类为“高亲合力”抗体或“低亲合力”抗体。“高亲合力”抗体是指 K_a 为至少 10^7M^{-1} 、至少 10^8M^{-1} 、至少 10^9M^{-1} 、至少 10^{10}M^{-1} 、至少 10^{11}M^{-1} 、至少 10^{12}M^{-1} 或至少 10^{13}M^{-1} 的那些抗体。“低亲合力”抗体是指 K_a 高达 10^7M^{-1} 、高达 10^6M^{-1} 、高达

10^5M^{-1} 的那些抗体。可选地,亲和力可以被定义为以M为单位的特定结合相互作用的平衡解离常数(K_d) (例如, 10^{-5}M 至 10^{-13}M)。

[0079] 已知用于鉴定结合特定靶标的本公开内容的抗体,以及确定结合结构域或结合蛋白亲和力的多种测定,例如蛋白质印迹、ELISA、分析超速离心、光谱学和表面等离子体共振(Biacore®)分析(参见,例如,Scatchard等人,Ann.N.Y.Acad.Sci.51:660,1949;Wilson, Science295:2103,2002;Wolff等人,Cancer Res.53:2560,1993;和美国专利第5,283,173号、第5,468,614号,或其等同物)。用于评估亲和力或表观亲和力或相对亲和力的测定也是已知的。在某些实例中,通过评估与各种浓度的四聚体的结合,例如通过使用标记的四聚体的流式细胞术来测量免疫球蛋白结合蛋白的表观亲和力。在一些实例中,免疫球蛋白结合蛋白的表观 K_d 使用一定浓度范围的标记四聚体的2倍稀释液来测量,然后通过非线性回归确定结合曲线,表观 K_d 被确定为产生半数最大结合的配体的浓度。

[0080] 在某些实施方案中,本公开内容的抗体或抗原结合片段能够在体外细胞运动性测定中降低弯曲杆菌的运动性。在图2中示意性地示出了示例性运动性测定;还参见Riazi等人,PLoS One 8(12):e83928(2013)。

[0081] 在某些实施方案中,本公开内容的抗体能够中和一种或多种弯曲杆菌的感染。如本文所用,“中和抗体”是可以中和,即,预防、抑制、降低、阻止或干扰病原体在宿主中引发和/或持续感染的能力的抗体。术语“中和抗体”和“中和……的一种抗体”或“中和……的多种抗体”在本文中可互换使用。

[0082] 在任何目前公开的实施方案中,弯曲杆菌包括空肠弯曲杆菌、大肠弯曲杆菌或两者。在某些实施方案中,弯曲杆菌包括空肠弯曲杆菌81-176、大肠弯曲杆菌10092/ATB或两者。

[0083] 除非在本文中有不同的明确定义,否则抗体技术领域的技术人员所理解的术语各自给出了本领域所获得的含义。例如,术语“抗体”是指包含通过二硫键相互连接的至少两条重(H)链和两条轻(L)链的完整抗体,以及完整抗体的任何抗原结合部分或片段,其具有或保留了结合完整抗体识别的抗原靶标分子的能力,例如scFv、Fab或Fab'2片段。因此,术语“抗体”在本文中以最广泛的意义使用,并且包括多克隆抗体和单克隆抗体,其包括完整抗体及其功能(抗原结合)抗体片段,包括抗原结合(Fab)片段,F(ab')2片段,Fab'片段,Fv片段,重组IgG(rIgG)片段,单链抗体片段,包括单链可变片段(scFv)和单结构域抗体(例如,sdAb、sdFv、纳米抗体)片段。该术语涵盖免疫球蛋白的基因工程改造和/或其它修饰形式,例如胞内抗体(intrabodies),肽体,嵌合抗体,全人抗体,人源化抗体和异缀合抗体,多特异性抗体,例如双特异性抗体、双链抗体、三链抗体、四链抗体、串联双scFv和串联三scFv。除非另有说明,否则术语“抗体”应理解为涵盖其功能抗体片段。该术语还涵盖完整抗体或全长抗体,其包括任何类别或亚类的抗体,包括IgG及其亚类,IgM、IgE、IgA和IgD。

[0084] 术语“ V_L ”或“VL”和“ V_H ”或“VH”分别指抗体轻链和重链的可变结合区。在某些实施方案中,VL是 κ 类别(本文也称为“VK”)。在某些实施方案中,VL是 λ 类别。可变结合区由称为“互补决定区”(CDR)和“框架区”(FR)的离散的、定义明确的子区组成。术语“互补决定区”和“CDR”与“高变区”或“HVR”同义,并且是指抗体可变区内的氨基酸序列,其通常赋予抗体的抗原特异性和/或结合亲和力,并且通过框架区彼此分开。在每个可变区中有三个CDR(HCDR1、HCDR2、HCDR3;LCDR1、LCDR2、LCDR3;也分别称为CDRH和CDRL)。在某些实施方案中,

抗体VH包含如下四个FR和三个CDR:FR1-HCDR1-FR2-HCDR2-FR3-HCDR3-FR4;以及抗体VL包含如下的四个FR和三个CDR:FR1-LCDR1-FR2-LCDR2-FR3-LCDR3-FR4。通常,VH和VL通过它们各自的CDR一起形成抗原结合位点。

[0085] 如本文所用,CDR的“变体”是指具有多达1-3个氨基酸取代(例如保守或非保守取代)、缺失或其组合的CDR序列的功能变体。

[0086] CDR和框架区的编号可以根据任何已知的方法或方案,例如Kabat、Chothia、EU、IMGT和AHO编号方案(参见,例如,Kabat等人,“Sequences of Proteins of Immunological Interest,US Dept.Health and Human Services,Public Health Service National Institutes of Health,1991,第5版;Chothia和Lesk,J.Mol.Biol.196:901-917(1987));Lefranc等人,Dev.Comp.Immunol.27:55,2003;Honegger和Plückthun,J.Mol.Bio.309:657-670(2001))。可以使用抗原受体编号和受体分类(ANARCI)软件工具(2016,Bioinformatics 15:298-300)对待比较的不同分子的等同残基位置进行注释。

[0087] 在某些实施方案中,本公开内容的抗体或抗原结合片段包含(i)分别根据SEQ ID NO:9-14的HCDR1、HCDR2、HCDR3、LCDR1、LCDR2和LCDR3氨基酸序列;或者(ii)分别根据SEQ ID NO:25-30的HCDR1、HCDR2、HCDR3、LCDR1、LCDR2和LCDR3氨基酸序列。

[0088] 术语“CL”是指“免疫球蛋白轻链恒定区”或“轻链恒定区”,即来自抗体轻链的恒定区。术语“CH”是指“免疫球蛋白重链恒定区”或“重链恒定区”,其根据抗体同种型可进一步分成CH1、CH2和CH3(IgA、IgD、IgG)或者CH1、CH2、CH3和CH4结构域(IgE、IgM)。

[0089] “Fab”(抗原结合片段)是与抗原结合的抗体的一部分,包括通过链间二硫键与轻链连接的重链的可变区和CH1。每个Fab片段在抗原结合方面是单价的,即它具有单一抗原结合位点。对抗体进行胃蛋白酶处理产生单个大的F(ab')₂片段,其大致对应于具有二价抗原结合活性的两个二硫化物连接的Fab片段,并且仍能够交联抗原。Fab和F(ab')₂均是“抗原结合片段”的实例。Fab'片段与Fab片段的不同之处在于在CH1结构域的羧基末端具有另外的少量残基,包括来自抗体铰链区的一个或多个半胱氨酸。Fab'-SH是本文中Fab'的名称,其中恒定结构域中的半胱氨酸残基带有游离硫醇基团。F(ab')₂抗体片段最初作为Fab'片段对产生,它们之间具有铰链半胱氨酸。抗体片段的其它化学偶联也是已知的。

[0090] “Fv”是含有完整抗原识别和抗原结合位点的最小抗体片段。该片段由紧密非共价缔合的一个重链和一个轻链可变区结构域的二聚体组成。从这两个结构域的折叠产生六个高变环(三个环各自来自H链和L链),其为抗原结合贡献氨基酸残基并赋予抗体抗原结合特异性。然而,即使单个可变结构域(或仅包含三个对抗原具有特异性的CDR的Fv的一半)也具有识别和结合抗原的能力,尽管亲和力通常低于完整结合位点。

[0091] “单链Fv”也缩写为“sFv”或“scFv”,是包含连接到单个多肽链中的V_H和V_L抗体结构域的抗体片段。优选地,sFv多肽还包含V_H和V_L结构域之间的多肽接头,其使得sFv能够形成抗原结合的期望结构。关于sFv的综述,参见Plückthun in The Pharmacology of Monoclonal Antibodies,第113卷,Rosenburg和Moore编辑,Springer-Verlag,New York,pp.269-315(1994);Borrebaeck 1995,见下文。

[0092] 在抗体开发过程中,种系变量(V)、连接(J)和多样性(D)基因座中的DNA可以被重排,并且可以在编码序列中发生核苷酸的插入和/或缺失。体细胞突变可以由所得序列编码,并且可以通过参考相应的已知种系序列来鉴定。在一些情况下,体细胞突变可以用相应

的种系编码的氨基酸或不同的氨基酸代替,从而改善或维持抗体的期望特性,并降低或消除抗体的不期望特性,所述体细胞突变对于抗体的期望特性(例如,特异性结合弯曲杆菌)不是关键的,或者赋予抗体不期望的特性(例如,在施用抗体的对象中增加的免疫原性风险)或者两者。因此,在一些实施方案中,与亲本抗体或抗原结合片段相比,本公开内容的抗体或抗原结合片段在可变区中包含至少一个以上种系编码的氨基酸,条件是所述亲本抗体或抗原结合片段包含一个或多个体细胞突变。本文表1中提供了本公开内容的示例性抗弯曲杆菌抗体的可变区氨基酸序列,其中体细胞突变由下划线显示。

[0093] 本文还提供了与目前公开的(“亲本”)抗体相比在可变区(例如VH、VL、框架或CDR)中包含一个或多个氨基酸改变的变体抗体,其中所述变体抗体能够以类似于或强于亲本抗体的亲和力特异性结合弯曲杆菌F1iD表位。例如,在一些实施方案中,本公开内容的抗体或抗原结合片段包含与SEQ ID NO:2或22的氨基酸序列具有至少70%、75%、80%、85%、90%、91%、92%、93%、94%、95%、96%、97%、98%或至少99%的序列同一性的重链可变结构域(VH)以及与SEQ ID NO:4或24的氨基酸序列具有至少70%、75%、80%、85%、90%、91%、92%、93%、94%、95%、96%、97%、98%或至少99%的序列同一性的轻链可变结构域(VL),条件是变体抗体或抗原结合片段以类似于或优于亲本抗体的亲和力特异性结合弯曲杆菌F1iD表位,所述亲本抗体分别具有根据SEQ ID NO:2或22的VH和根据SEQ ID NO:4或24的VL。

[0094] 在某些实施方案中,抗体或抗原结合片段可以包含:(i)与SEQ ID NO:2具有至少85%(即,至少85%、86%、87%、88%、89%、90%、91%、92%、93%、94%、95%、96%、97%、98%、99%或更多)的氨基酸同一性的VH以及与SEQ ID NO:4具有至少85%(即,至少85%、86%、87%、88%、89%、90%、91%、92%、93%、94%、95%、96%、97%、98%、99%或更多)的氨基酸同一性的VL;或者(ii)与SEQ ID NO:22具有至少85%的氨基酸同一性的VH以及与SEQ ID NO:24具有至少85%的氨基酸同一性的VL。

[0095] 在进一步的实施方案中,抗体或抗原结合片段包含:(i)根据SEQ ID NO:2的VH以及根据SEQ ID NO:4的VL;或者(ii)根据SEQ ID NO:22的VH以及根据SEQ ID NO:24的VL。

[0096] 在任何目前公开的实施方案中,抗体或抗原结合片段是多特异性的;例如,双特异性的、三特异性的等。

[0097] 在任何目前公开的实施方案中,抗体或抗原结合片段是IgA、IgG、IgD、IgE或IgM同种型。

[0098] 在某些实施方案中,抗体或抗原结合片段是IgA同种型。在人类中,发现IgA抗体呈单体、二聚体或四聚体形式。IgA亚类包括IgA1和IgA2。IgA1具有比IgA2更长的铰链序列(在Fab臂与Fc之间)。参见,例如,Woof和Kerr, *Immunology* 113(2):175-177(2004)。

[0099] 不希望受理论的束缚,IgA二聚体通常包含通过在IgA分泌细胞中形成的至少一条连接链(“J-链”)多肽连接在一起的两个IgA单体。可溶性IgA二聚体通常能够与在上皮细胞的基底外侧表面上发现的聚-Ig受体(“pIgR”)蛋白形成复合物。形成后,IgA二聚体-pIgR复合物被内化到上皮细胞中并转运到腔表面以释放到腔中。在分泌到腔中之前,一部分pIgR被切割,而被称为“分泌成分”或“SC”的部分仍然与IgA结合,形成分泌型IgA(SIgA)。不希望受理论的束缚,认为SC可以通过保护IgA二聚体中的蛋白水解敏感位点来改善IgA二聚体在囊泡和腔环境中的稳定性。

[0100] 在某些实施方案中,本公开内容的抗体或抗原结合片段是IgA1同种型或IgA2同种型。

[0101] 在某些实施方案中,本公开内容的抗体或抗原结合片段包含IgA二聚体分子。

[0102] 在某些实施方案中,本公开内容的抗体或抗原结合片段包含分泌型IgA分子。

[0103] “Fc”片段或Fc多肽包含通过二硫化物连接在一起的抗体H链的羧基末端部分(即IgG的CH2结构域和CH3结构域)。抗体的效应子功能由Fc区中的序列决定。Fc结构域是细胞受体例如FcR识别并且补体激活蛋白C1q结合的抗体部分。如本文讨论的,可以对Fc结构域进行修饰(例如,氨基酸取代),以修饰(例如,改善、减少或消除)含Fc多肽(例如,本公开内容的抗体)的一种或多种功能。在任何目前公开的实施方案中,抗体或抗原结合片段包含Fc多肽或其片段,其包括CH2(或其片段)、CH3(或其片段)或者CH2和CH3,其中CH2、CH3或两者可以是任何同种型,并且分别与相应的野生型CH2或CH3相比可以含有氨基酸取代或其它修饰。在某些实施方案中,本公开内容的Fc多肽包含缔合以形成二聚体的两条CH2-CH3多肽。

[0104] 在某些实施方案中,抗体或抗原结合片段包含与SEQ ID NO:40-42中的任一项具有至少90%的同一性(即,至少90%、91%、92%、93%、94%、95%、96%、97%、98%或至少99%的序列同一性)的重链恒定区。

[0105] 在任何目前公开的实施方案中,抗体或抗原结合片段是单克隆的。本文所用的术语“单克隆抗体(mAb)”是指从基本上均质的抗体群体中获得的抗体,即,除了在一些情况下可能存在少量的可能天然存在的突变外,包含该群体的各个抗体是相同的。单克隆抗体针对单一抗原位点具有高度特异性。此外,与包括针对不同表位的不同抗体的多克隆抗体制备物相反,每种单克隆抗体对抗原的单一表位。除了单克隆抗体的特异性外,单克隆抗体的优点在于它们可以被合成而不被其它抗体污染。术语“单克隆的”不应被解释为需要通过任何特定方法产生抗体。例如,可用于本发明的单克隆抗体可以通过Kohler等人,Nature 256:495(1975)首次描述的杂交瘤方法制备,或者可以使用重组DNA方法在细菌、真核动物或植物细胞中制备(参见,例如,美国专利第4,816,567号)。单克隆抗体也可以使用例如Clackson等人,Nature,352:624-628(1991)和Marks等人,J.Mol.Biol.,222:581-597(1991)中所述的技术从噬菌体抗体库中分离。单克隆抗体也可以使用PCT公开号WO 2004/076677A2中公开的方法获得。

[0106] 本公开内容的抗体和抗原结合片段包括“嵌合抗体”,其中重链和/或轻链的一部分与衍生自特定物种或属于特定抗体类别或亚类的抗体中的相应序列相同或同源,而链的其余部分与衍生自另一物种或属于另一抗体类别或亚类的抗体中的相应序列相同或同源,以及此类抗体的片段,只要它们表现出期望的生物活性(参见美国专利第4,816,567号;第5,530,101号和第7,498,415号;以及Morrison等人,Proc.Natl.Acad.Sci.USA,81:6851-6855(1984))。例如,嵌合抗体可以包含人类和非人类残基。此外,嵌合抗体可以包含接受者抗体或供体抗体中未发现的残基。进行这些修饰以进一步改善抗体性能。关于进一步的细节,参见Jones等人,Nature 321:522-525(1986);Riechmann等人,Nature332:323-329(1988);以及Presta,Curr.Op.Struct.Biol.2:593-596(1992)。嵌合抗体还包括灵长类化(primatized)抗体和人源化抗体。

[0107] “人源化抗体”通常被认为是具有从非人类来源引入一个或多个氨基酸残基的人类抗体。这些非人类氨基酸残基通常取自可变结构域。可以按照Winter和同事的方法

(Jones等人, Nature, 321:522-525 (1986); Reichmann等人, Nature, 332:323-327 (1988); Verhoeyen等人, Science, 239:1534-1536 (1988)), 通过用非人类可变序列取代人类抗体的相应序列进行人源化。因此, 此类“人源化”抗体是嵌合抗体(美国专利第4,816,567号; 第5,530,101号和第7,498,415号), 其中基本上少于完整的人类可变结构域已经被来自非人类物种的相应序列取代。在一些情况下, “人源化”抗体是由非人类细胞或动物产生并且包含人类序列, 例如H_c结构域的抗体。

[0108] “人类抗体”是仅含有存在于由人类产生的抗体中的序列的抗体。然而, 如本文所用, 人类抗体可以包含在天然存在的人类抗体(例如, 从人类中分离的抗体)中未发现的残基或修饰, 其包括本文所述的那些修饰和变体序列。通常产生这些以进一步改善或增强抗体性能。在一些情况下, 人类抗体是由转基因动物产生的。例如, 参见美国专利第5,770,429号; 第6,596,541号和第7,049,426号。

[0109] 在某些实施方案中, 本公开内容的抗体或抗原结合片段是嵌合的、人源化的或人类的。

[0110] 本文还提供了包含本文公开的任何抗体或抗原结合片段以及药学上可接受的载体、赋形剂或稀释剂的组合物。本文还讨论了用于此类组合物中的药学上可接受的组分。

[0111] 在另一方面, 本公开内容提供了试剂盒, 其中试剂盒包含: (i) 第一抗体或其抗原结合片段, 所述第一抗体或其抗原结合片段对弯曲杆菌鞭毛加帽蛋白(FliD)线性表位具有特异性; 以及(ii) 第二抗体或其抗原结合片段, 所述第二抗体或其抗原结合片段对弯曲杆菌鞭毛加帽蛋白(FliD)构象表位具有特异性。

[0112] 在某些实施方案中, (i) 第一抗体或抗原结合片段包含分别根据SEQ ID NO:9-14的HCDR1、HCDR2、HCDR3、LCDR1、LCDR2和LCDR3序列; 以及(ii) 第二抗体或抗原结合片段包含分别根据SEQ ID NO:25-30的HCDR1、HCDR2、HCDR3、LCDR1、LCDR2和LCDR3序列。

[0113] 在某些实施方案中, (i) 第一抗体或抗原结合片段包含与SEQ ID NO:2具有至少85%的氨基酸同一性的VH以及与SEQ ID NO:4具有至少85%的氨基酸同一性的VL; 以及(ii) 第二抗体或抗原结合片段包含与SEQ ID NO:22具有至少85%的氨基酸同一性的VH, 以及与SEQ ID NO:24具有至少85%的氨基酸同一性的VL。在进一步的实施方案中: (i) 第一抗体或抗原结合片段包含根据SEQ ID NO:2的VH和根据SEQ ID NO:4的VL; 以及(ii) 第二抗体或抗原结合片段包含根据SEQ ID NO:22的VH和根据SEQ ID NO:24的VL。

[0114] 在某些实施方案中, 试剂盒中的第一抗体或抗原结合片段以及第二抗体或抗原结合片段各自是相同的同种型。在特定的实施方案中, 第一抗体或抗原结合片段以及第二抗体或抗原结合片段各自是分泌型IgA。

[0115] 在某些实施方案中, 试剂盒还包含关于使用第一抗体和第二抗体或抗原结合片段, 例如, 以治疗或诊断对象中的弯曲杆菌感染的用法说明书或使用说明。

[0116] 多核苷酸、载体和宿主细胞

[0117] 在另一个方面, 本公开内容提供了编码任何目前公开的抗体或其抗原结合片段的分离的多核苷酸。在某些实施方案中, 多核苷酸是密码子优化的, 用于在宿主细胞中表达。一旦已知或鉴定了编码序列, 就可以使用已知的技术和工具, 例如使用 **GenScript®** **OptimumGene™** 工具进行密码子优化; 还参见Scholten等人, Clin. Immunol. 119:135, 2006。密码子优化的序列包括部分是密码子优化的序列(即, 一个或多个密码子被优化用于在宿

主细胞中表达)和完全密码子优化的序列。

[0118] 还应理解,编码本公开内容的抗体和抗原结合片段的多核苷酸可以具有不同的核苷酸序列,而由于例如遗传密码的简并性、剪接等仍然编码相同的抗体或抗原结合片段。

[0119] 在某些实施方案中,编码F1iD特异性抗体或抗原结合片段的分离的多核苷酸包含:(i) 编码VH的多核苷酸,其与SEQ ID NO:1、5、7、8、21、37或38中任一项所示的核苷酸序列具有至少75%的同一性(即,至少75%、80%、85%、90%、91%、92%、93%、94%、95%、96%、97%、98%或至少99%的序列同一性);(ii) 编码VL的多核苷酸,其与SEQ ID NO:3、6、23或39所示的核苷酸序列具有至少75%的同一性;和/或(iii) 编码HCDR1-、HCDR2-、HCDR3-、LCDR1-、LCDR2-和LCDR3-的序列,其分别与SEQ ID NO:15-20或分别与SEQ ID NO:31-36所示的核苷酸序列具有至少90%的同一性。

[0120] 还提供了载体,其中所述载体包含或含有本文公开的多核苷酸(即,编码F1iD特异性抗体或抗原结合片段的多核苷酸)。载体可以包含本文公开的任何一种或多种载体。

[0121] 在另一方面,本公开内容还提供了表达根据本公开内容的抗体或抗原结合片段的宿主细胞;或者包含或含有根据本公开内容的载体或多核苷酸的宿主细胞。

[0122] 此类细胞的实例包括但不限于真核细胞,例如酵母细胞、动物细胞、昆虫细胞、植物细胞;以及原核细胞,包括大肠杆菌。在一些实施方案中,细胞是哺乳动物细胞。在某些这样的实施方案中,细胞是哺乳动物细胞系,例如CHO细胞(例如,DHFR-CHO细胞(Urlaub等人,PNAS 77:4216(1980))、人胚肾细胞(例如HEK293T细胞)、PER.C6细胞、Y0细胞、Sp2/0细胞、NS0细胞、人肝细胞(例如Hepa RG细胞)、骨髓瘤细胞或杂交瘤细胞。哺乳动物宿主细胞系的其它实例包括小鼠塞托利细胞(例如,TM4细胞);通过SV40转化的猴肾CV1系(COS-7);幼仓鼠肾细胞(BHK);非洲绿猴肾细胞(VERO-76);猴肾细胞(CV1);人宫颈癌细胞(HELA);人肺细胞(W138);人肝细胞(Hep G2);犬肾细胞(MDCK;布法罗大鼠肝细胞(buffalo rat liver cells)(BRL 3A);小鼠乳腺肿瘤(MMT 060562);TRI细胞;MRC 5细胞;和FS4细胞。适用于抗体产生的哺乳动物宿主细胞系还包括在例如Yazaki和Wu,Methods in Molecular Biology,第248卷(B.K.C.Lo编辑,Humana Press,Totowa,N.J.),pp.255-268(2003)中描述的那些。

[0123] 在某些实施方案中,宿主细胞是原核细胞,例如大肠杆菌。肽在原核细胞如大肠杆菌中的表达已被很好地确立(参见,例如,Pluckthun,A.Bio/Technology 9:545-551(1991))。例如,可以在细菌中产生抗体,特别是当不需要糖基化和Fc效应子功能时。关于抗体片段和多肽在细菌中的表达,参见例如美国专利第5,648,237号;第5,789,199号和第5,840,523号。

[0124] 在特定的实施方案中,可以用根据本说明书的载体,用表达载体转染细胞。术语“转染”是指将核酸分子,例如DNA或RNA(例如mRNA)分子引入细胞,例如真核细胞。在本说明书的上下文中,术语“转染”涵盖本领域技术人员已知的用于将核酸分子引入细胞,例如真核细胞,包括哺乳动物细胞的任何方法。此类方法涵盖,例如,电穿孔,脂质转染(例如基于阳离子脂质和/或脂质体),磷酸钙沉淀,基于纳米颗粒的转染,基于病毒的转染或基于阳离子聚合物的转染,例如DEAE-葡聚糖或聚乙烯亚胺等。在某些实施方案中,引入是非病毒的。

[0125] 此外,可以用根据本公开内容的载体(例如用于表达根据本公开内容的抗体或其抗原结合片段)稳定地或瞬时地转染本公开内容的宿主细胞。在这样的实施方案中,可以用

本文所述的载体稳定地转染细胞。可选地,可以用根据本公开内容的编码本文公开的抗体或抗原结合片段的载体瞬时地转染细胞。在任何目前公开的实施方案中,多核苷酸可以是宿主细胞异源的。

[0126] 因此,本公开内容还提供了异源表达本公开内容的抗体或抗原结合片段的重组宿主细胞。例如,细胞可以是与完全或部分获得抗体的物种(例如,表达人类抗体或工程改造的人类抗体的CHO细胞)不同的物种。在一些实施方案中,宿主细胞的细胞类型在自然界中不表达抗体或抗原结合片段。此外,宿主细胞可以赋予抗体或抗原结合片段的翻译后修饰(PTM;例如,糖基化或岩藻糖基化),其不存在于抗体或抗原结合片段的天然状态(或亲本抗体的天然状态,从所述亲本抗体工程改造或衍生成抗体或抗原结合片段)中。此类PTM可导致功能差异(例如,降低的免疫原性)。因此,如本文公开的由宿主细胞产生的本公开内容的抗体或抗原结合片段可以包括一种或多种翻译后修饰,其不同于天然状态的抗体(或亲本抗体)(例如,由CHO细胞产生的人类抗体可以包含更多的翻译后修饰,其不同于当从人类分离和/或由天然人类B细胞或浆细胞产生的抗体)。

[0127] 可用于表达本公开内容的结合蛋白的昆虫细胞是本领域已知的,并且包括,例如, *Spodoptera frugiper*a Sf9细胞、粉纹夜蛾(*Trichoplusia ni*) BTI-TN5B1-4细胞和 *Spodoptera frugiper*a SfSWT01“MimicTM”细胞。参见,例如, Palmberger等人, *J. Biotechnol.* 153(3-4):160-166(2011)。已经鉴定了许多杆状病毒毒株,其可以与昆虫细胞结合使用,特别是用于转染草地贪夜蛾(*Spodoptera frugiperda*)细胞。

[0128] 真核微生物例如丝状真菌或酵母也是用于克隆或表达编码蛋白质的载体的合适宿主,并且包括具有“人源化”糖基化途径的真菌和酵母菌株,导致产生具有部分或完全人类糖基化模式的抗体。参见 Gerngross, *Nat. Biotech.* 22:1409-1414(2004); Li等人, *Nat. Biotech.* 24:210-215(2006)。

[0129] 植物细胞也可以用作表达本公开内容的结合蛋白的宿主。例如, PLANTIBODIESTM技术(描述于例如美国专利第5,959,177号;第6,040,498号;第6,420,548号;第7,125,978号;和第6,417,429号)使用转基因植物产生抗体。

[0130] 在某些实施方案中,宿主细胞包括哺乳动物细胞。在特定的实施方案中,宿主细胞是CHO细胞、HEK293细胞、PER.C6细胞、Y0细胞、Sp2/0细胞、NS0细胞、人肝细胞、骨髓瘤细胞或杂交瘤细胞。

[0131] 在相关方面,本公开内容提供了用于产生抗体、抗原结合片段的方法,其中所述方法包括将本公开内容的宿主细胞在足以产生所述抗体或所述抗原结合片段的条件下和时间段培养。例如,可用于分离和纯化重组产生的抗体的方法可以包括从将重组抗体分泌到培养基中的合适宿主细胞/载体系统中获得上清液,然后使用可商购获得的过滤器浓缩培养基。浓缩后,可以将浓缩物施加到单一合适的纯化基质或一系列合适的基质,例如亲和基质或离子交换树脂。可以使用一个或多个反相HPLC步骤来进一步纯化重组多肽。当从免疫原的天然环境中分离免疫原时,也可以使用这些纯化方法。用于大规模生产本文所述的一种或多种分离的抗体/重组抗体的方法包括分批细胞培养,对其进行监测和控制以维持适当的培养条件。可溶性抗体的纯化可以根据本文所述和本领域已知的且符合国内外管理机构的法律和指南的方法进行。

[0132] 弯曲杆菌感染模型

[0133] 在另一方面,本公开内容提供了用于研究弯曲杆菌感染和发病机理的动物模型,以及潜在的疗法和研究试剂。

[0134] 简而言之,用于研究弯曲杆菌发病机理的现有动物模型具有许多缺点,例如高成本和重症监护环境(例如,悉生动物或无菌动物),对弯曲杆菌肠道定植的抗性(例如,实验室小鼠)以及转基因动物(例如,SIGIRR或IL10^{-/-}小鼠)的不可预知的或有害的作用。如实施例所述,发现不再接受母体抗体但不具有成熟的胃肠道免疫系统并具有耗损的肠道菌群的最接近断奶动物(21日龄小鼠),令人惊讶地易受弯曲杆菌感染的影响;因此,提供了用于研究弯曲杆菌发病机理及其潜在治疗的改进模型。

[0135] 在某些实施方案中,提供了非人类哺乳动物,其中所述非人类哺乳动物包含断奶的哺乳动物,所述断奶的哺乳动物:(i)不具有成熟的胃肠道免疫系统,以及(ii)具有耗损的肠道菌群,其中所述耗损由抗生素药剂导致。在某些实施方案中,非人类哺乳动物还包含弯曲杆菌感染。

[0136] 在某些实施方案中,本公开内容的非人类哺乳动物是或包含小鼠(例如,C57BL/6小鼠)、大鼠、猪、兔、狗、猫、豚鼠、仓鼠、非人类灵长类(例如,猕猴)等。已经断奶的非人类哺乳动物不再通过奶从母体哺乳动物(即,生下非人类哺乳动物的母体或代孕母体)接受营养物。

[0137] 根据本公开内容的成熟胃肠道免疫系统是能够针对抗原或病原体发挥功能性内源性免疫活性(例如粘膜保护)的系统。例如,成熟的胃肠道免疫系统通过微皱褶细胞、树突细胞和巨噬细胞处理抗原以呈递给肠道相关淋巴组织中的T细胞,并通过B细胞产生抗原中和IgA免疫球蛋白。参见,例如,Gutzeit等人,Immunol.Rev.260(2):76-85(2014)。在某些实施方案中,与处于胃肠道免疫系统被认为是成熟的和功能性的年龄和/或发育阶段的参照健康非人类哺乳动物(即相同物种的)相比,本文公开的非人类哺乳动物不会内源地产生IgA免疫球蛋白,或者产生减少量的IgA免疫球蛋白。在健康的动物中,成熟的胃肠道免疫系统通常会随着年龄自然出现;例如,健康成年小鼠(56天)具有成熟的胃肠道免疫系统。

[0138] 应理解,共生细菌(也统称为“菌群”或“微生物群”)栖息在肠中,赋予宿主各种防御和代谢能力(参见Gutzeit等人,Immunol.Rev.260(2):76-85(2014))。该菌群可以防止或抑制病原体(例如弯曲杆菌)的定植。耗损的肠道菌群是与健康参照非人类哺乳动物(即相同物种和相同年龄的或大约相同年龄的)的肠道菌群相比,在以下中的一种或多种具有统计学上显著减少的菌群:细菌的总数;一种或多种细菌的生长速率;细菌的代谢功能;细菌的防御功能;和/或细菌多样性。

[0139] 此类非人类哺乳动物可以通过与母体分离而断奶的年龄或发育阶段将符合相关的动物护理标准和有机体的已知生物学。例如,小鼠可以在出生后约15天、约16天、约17天、约18天、约19天、约20天、约21天、约22天、约23天、约24天、约25天、约26天、约27天、约28天、约29天或约30天断奶,或之后断奶。在某些实施方案中,断奶的小鼠是18日龄、19日龄、20日龄、21日龄、22日龄、23日龄或24日龄或以上。在某些实施方案中,选择处于这样的年龄或发育阶段的非人类哺乳动物,所述年龄或发育阶段分别小于或早于非人类哺乳动物将具有成熟胃肠道免疫系统的年龄或发育阶段。在其它实施方案中,可以对非人类哺乳动物进行操纵(例如,遗传或以其它方式)以延迟或预防成熟胃肠道免疫系统的发展。应理解,胃肠道免疫系统可以随着时间推移而成熟;因此,在优选的实施方案中,非人类哺乳动物是最近断奶

的。最近断奶的哺乳动物是已经断奶约1天至约10天的哺乳动物。

[0140] 根据本公开内容的非人类哺乳动物具有耗损的肠道菌群。使用本领域普通技术人员已知的方法,可以确定细菌数量、生长速率、代谢功能、防御功能和多样性,并与参照进行比较。

[0141] 可以例如通过施用抗生素药剂耗损肠道菌群。示例性的抗生素药剂包括万古霉素和其它糖肽抗生素、甲氧苄啶、氨苄青霉素、甲硝唑和链霉素、及其类似物、及其组合。在优选的实施方案中,抗生素药剂是或包含弯曲杆菌对其具有抗性的药剂;例如,万古霉素或其类似物。耗损肠道菌群的抗生素药剂的给药和施用可以考虑例如非人类哺乳动物的年龄、大小和/或健康以及期望的效果根据已知的原则来确定。

[0142] 在进一步的实施方案中,非人类哺乳动物还包含弯曲杆菌(例如,目的弯曲杆菌,例如空肠弯曲杆菌、大肠弯曲杆菌或两者)。弯曲杆菌可以例如以足以在肠中形成集落的量经口(例如通过灌胃)施用。例如,用 10^8 至 10^9 个弯曲杆菌接种12日龄、21日龄或56日龄的小鼠。在某些实施方案中,引入非人类哺乳动物中的弯曲杆菌包含约 10^5 、约 5×10^5 、约 10^6 、约 5×10^6 、约 10^7 、约 5×10^7 、约 10^8 、约 5×10^8 、约 10^9 、约 5×10^9 、约 10^{10} 、约 5×10^{10} 、约 10^{11} 、约 5×10^{11} 或约 10^{12} 个弯曲杆菌或更多。一旦施用,弯曲杆菌的数量可以在非人类哺乳动物宿主中生长到更大的数量。

[0143] 在相关方面,提供了方法,其包括以足以在非人类哺乳动物中引起肠道感染的量将弯曲杆菌施用至或用弯曲杆菌接种断奶的非人类哺乳动物,所述断奶的非人类哺乳动物(i)不具有成熟的胃肠道免疫系统,以及(ii)具有耗损的肠道菌群。

[0144] 在另一个方面,提供了方法,其包括向(i)断奶以及(ii)不具有成熟胃肠道免疫系统的非人类哺乳动物施用耗损非人类哺乳动物的肠道菌群的药剂。在某些实施方案中,所述药剂包括如本文公开的抗生素药剂,例如万古霉素或其类似物。在某些实施方案中,所述方法还包括以足以在非人类哺乳动物中引起包含弯曲杆菌的肠道感染的量将弯曲杆菌施用至非人类哺乳动物或用弯曲杆菌接种非人类哺乳动物。

[0145] 方法和用途

[0146] 本文还提供了使用本公开内容的抗体或抗原结合片段或者包含其的组合物治疗对象的方法,其中所述对象已经、被认为具有弯曲杆菌感染或处于患有弯曲杆菌感染的风险中。“治疗(treat)”、“治疗(treatment)”或“改善”是指对象(例如,人类或非人类哺乳动物,如灵长类、马、猫、狗、山羊、小鼠或大鼠)的疾病、病症或病况的医学管理。通常,包含本公开内容的抗体或组合物的适当剂量或治疗方案以足以引起治疗或预防益处的量施用。治疗或预防/防止益处包括改善的临床结果;减少或减轻与疾病相关的症状;减少症状的发生;提高生活质量;较长的无病状态;减少疾病的程度,稳定疾病状态;延缓疾病进展;缓解;存活;延长存活;或其任何组合。

[0147] 本公开内容的抗体、抗原结合片段或组合物的“治疗有效量”或“有效量”是指足以以统计学上显著的方式导致治疗效果,包括改善的临床结果;减少或减轻与疾病相关的症状;减少症状的发生;提高生活质量;较长的无病状态;减少疾病的程度,稳定疾病状态;延缓疾病进展;缓解;存活;或延长存活的组合物或分子的量。当涉及单独施用的单独活性成分时,治疗有效量是指该成分或表达该单独成分的细胞的作用。当涉及组合时,治疗有效量是指导致治疗效果的活性成分或组合的辅助活性成分与表达活性成分的细胞的组合量,不

管是依次、相继或同时施用。组合可以包含例如特异性结合弯曲杆菌表位(例如Flid表位)的两种不同的抗体,在某些实施方案中,所述弯曲杆菌可以是相同或不同的弯曲杆菌和/或可以包含相同或不同的表位。

[0148] 因此,在某些实施方案中,提供了用于治疗对象中的弯曲杆菌感染的方法,其中所述方法包括向所述对象施用有效量的本文公开的抗体、抗原结合片段或组合物。

[0149] 在某些实施方案中,提供了用于减少(即,减少或完全消除)具有弯曲杆菌感染的对象中的肠道炎症的方法,其中所述方法包括向所述对象施用有效量的如本文所公开的抗体、抗原结合片段或组合物。

[0150] 在某些实施方案中,提供了用于增加具有弯曲杆菌感染的对象中的弯曲杆菌的肠道脱落的方法,其中所述方法包括向所述对象施用有效量的如本文所公开的抗体、抗原结合片段或组合物。

[0151] 在任何目前公开的实施方案中,抗体或抗原结合片段包含分泌型IgA分子。

[0152] 可以通过本公开内容治疗的对象通常是人和其它灵长类对象,例如用于兽医学目的的猴子和猿。其它模型有机体,例如小鼠和大鼠,也可以根据本公开内容进行治疗。在前述实施方案的任一个中,对象可以是人类对象。对象可以是男性或女性,并且可以是任何合适的年龄,包括婴幼儿、少年、青少年、成年人和老年对象。

[0153] 因此,施用目前公开的组合物的典型途径包括但不限于口服、局部、透皮、吸入、肠胃外、舌下、颊、直肠、阴道和鼻内。本文所用的术语“肠胃外”包括皮下注射、静脉内、肌内、胸骨内注射或输注技术。在某些实施方案中,施用包括通过选自口服、静脉内、肠胃外、胃内、胸膜内、肺内、直肠内、皮肤内、腹腔内、肿瘤内、皮下、局部、透皮、脑池内、鞘内、鼻内和肌内的途径施用。在特定的实施方案中,方法包括向对象口服施用抗体、抗原结合片段或组合物。

[0154] 根据本发明的某些实施方案的药物组合物被配制使得其中包含的活性成分在将所述组合物施用至患者时是生物可利用的。将施用至对象或患者的组合物可以采取一个或多个剂量单位的形式,其中例如,片剂可以是单个剂量单位,并且本文所述的气溶胶形式的抗体或抗原结合的容器可以容纳多个剂量单位。制备此类剂型的实际方法是本领域技术人员已知的或对于本领域技术人员将是显而易见的;例如,参见Remington: The Science and Practice of Pharmacy,第20版(Philadelphia College of Pharmacy and Science, 2000)。不管怎样,待施用的组合物将含有有效量的本公开内容的抗体或其抗原结合片段,用于治疗根据本文的教导目的疾病或病况。

[0155] 组合物可以是固体形式或液体形式。在一些实施方案中,载体是微粒,使得组合物是例如片剂或粉末形式。载体可以是液体,组合物可以是例如口服油、可注射液体或气雾剂,其可用于例如吸入施用。当旨在用于口服施用时,药物组合物优选为固体形式或液体形式,其中半固体、半液体、悬浮液和凝胶形式包括在本文认为是固体或液体的形式中。

[0156] 作为用于口服施用的固体组合物,可以将药物组合物配制成为粉末、颗粒、压缩片剂、丸剂、胶囊、口香糖、薄片(wafer)等。此类固体组合物通常含有一种或多种惰性稀释剂或可食用载体。此外,可以存在一种或多种以下物质:粘合剂,例如羧甲基纤维素、乙基纤维素、微晶纤维素、黄蓍胶或明胶;赋形剂,例如淀粉、乳糖或糊精;崩解剂,例如海藻酸、海藻酸钠、Primogel、玉米淀粉等;润滑剂,例如硬脂酸镁或Sterotex;助流剂,例如胶体二氧化

硅;甜味剂,例如蔗糖或糖精;调味剂,例如薄荷、水杨酸甲酯或橙子调味剂;和着色剂。当组合物为胶囊(例如明胶胶囊)的形式时,除了上述类型的材料之外,它还可以含有液体载体,例如聚乙二醇或油。

[0157] 组合物可以是液体形式,例如酞剂、糖浆、溶液、乳液或悬浮液。作为两个实例,液体可以用于口服施用或通过注射递送。当旨在用于口服施用时,除了本发明的化合物外,优选的组合物还含有甜味剂、防腐剂、染料/着色剂和增味剂中的一种或多种。在旨在通过注射施用的组合物中,可以包括表面活性剂、防腐剂、润湿剂、分散剂、悬浮剂、缓冲剂、稳定剂和等渗剂中的一种或多种。

[0158] 无论液体药物组合物是溶液、悬浮液或其它类似形式,所述液体药物组合物可以包括一种或多种以下佐剂:无菌稀释剂,例如注射用水,盐水溶液(优选生理盐水),林格氏溶液,等渗氯化钠,固定油,例如合成的甘油单酯或甘油二酯,其可以用作溶剂或悬浮介质,聚乙二醇,甘油,丙二醇或其它溶剂;抗菌剂,例如苄醇或对羟基苯甲酸甲酯;抗氧化剂,例如抗坏血酸或亚硫酸氢钠;螯合剂,例如乙二胺四乙酸;缓冲剂,例如乙酸盐、柠檬酸盐或磷酸盐,以及用于调节张力的试剂,例如氯化钠或右旋糖。肠胃外制剂可以封装在安瓿瓶、一次性注射器或者由玻璃或塑料制成的多剂量小瓶中。生理盐水是优选的佐剂。可注射的药物组合物优选是无菌的。

[0159] 旨在用于肠胃外或口服施用的液体组合物应含有一定量的本文公开的抗体或抗原结合片段,以便获得合适的剂量。通常,该量为组合物中抗体或抗原结合片段的至少0.01%。当旨在用于口服施用时,该量可以变化为组合物重量的0.1%至约70%。某些口服药物组合物含有约4%至约75%的抗体或抗原结合片段。在某些实施方案中,制备根据本发明的药物组合物和制剂,使得在稀释前肠胃外剂量单位含有0.01-10重量%的抗体或抗原结合片段。

[0160] 组合物可以旨在用于局部施用,在这种情况下,载体可以适当地包含溶液、乳液、软膏或凝胶基质。例如,所述基质可以包含一种或多种以下物质:凡士林、羊毛脂、聚乙二醇、蜂蜡、矿物油、稀释剂(如水和酒精)以及乳化剂和稳定剂。增稠剂可以存在于用于局部施用的组合物中。如果旨在用于透皮施用,则组合物可以包含透皮贴剂或离子电渗装置。药物组合物可以以例如栓剂的形式旨在用于直肠施用,该栓剂将在直肠中融化并释放药物。用于直肠施用的组合物可以含有油质基质作为合适的无刺激性赋形剂。此类碱包括但不限于羊毛脂、可可脂和聚乙二醇。

[0161] 组合物可以包括改变固体或液体剂量单位的物理形式的各种材料。例如,组合物可以包括在活性成分周围形成包衣壳的材料。形成包衣壳的材料通常是惰性的,并且可以选自例如糖、虫胶和其它肠溶包衣剂。可选地,可以将活性成分包装在明胶胶囊中。固体或液体形式的组合物可以包括与本公开内容的抗体或抗原结合片段结合并由此帮助递送化合物的试剂。可以在该能力中起作用的合适试剂包括单克隆抗体或多克隆抗体、一种或多种蛋白或脂质体。组合物可以基本上由可作为气雾剂施用的剂量单位组成。术语“气雾剂”用于表示范围为胶体性质的那些系统到由加压包装组成的系统的多种系统。递送可以通过液化或压缩气体或者通过分配活性成分的合适的泵系统进行。气雾剂可以在单相、双相或三相系统中递送以递送活性成分。气雾剂的递送包括必需的容器、活化剂、阀、子容器等,它们一起可以形成试剂盒。本领域普通技术人员无需过多的实验就可以确定优选的气雾剂。

[0162] 可以通过制药领域众所周知的方法制备药物组合物。例如,旨在通过注射施用的组合物可以通过将包含本文所述的抗体、其抗原结合片段或抗体缀合物以及任选的盐、缓冲剂和/或稳定剂中的一种或多种的组合物与无菌蒸馏水组合以形成溶液来制备。可以添加表面活性剂以促进均匀溶液或悬浮液的形成。表面活性剂是与肽组合物非共价相互作用以促进抗体或其抗原结合片段在水性递送系统中溶解或均匀悬浮的化合物。

[0163] 通常,适当的剂量和治疗方案以足以提供治疗和/或预防益处(如本文所述,包括改善的临床结果(例如,腹泻或相关脱水或炎症的频率、持续时间或严重程度的降低、或更长的无病和/或总体存活、或症状严重程度的减轻)的量提供组合物。对于预防使用,剂量应足以预防、延迟与疾病或病症相关的疾病的发作或者减轻其严重程度。根据本文所述方法施用的组合物的预防益处可以通过进行临床前(包括体外和体内动物研究)和临床研究以及通过适当的统计学、生物学和临床方法和技术(所有这些都可以由本领域技术人员容易地实践)分析由此获得的数据来确定。

[0164] 以有效量(例如,治疗弯曲杆菌感染)施用组合物,所述有效量将根据多种因素而变化,包括所用的具体化合物的活性;化合物的代谢稳定性和作用时间;对象的年龄、体重、一般健康状况、性别和饮食;施用方式和施用时间;排泄率;药物组合;特定病症或病况的严重程度;和经历治疗的对象。在某些实施方案中,与安慰剂治疗的或其它合适的对照对象相比,允许施用根据本公开内容的制剂和方法的治疗,测试对象将表现出与所治疗的疾病或病症相关的一种或多种症状减少约10%至约99%。

[0165] 通常,治疗有效的日剂量(对于70kg哺乳动物)为约0.001mg/kg(即0.07mg)至约100mg/kg(即7.0g);优选地,治疗有效剂量(对于70kg哺乳动物)为约0.01mg/kg(即0.7mg)至约50mg/kg(即3.5g);更优选地,治疗有效剂量(对于70kg哺乳动物)为约1mg/kg(即70mg)至约25mg/kg(即1.75g)。

[0166] 在某些实施方案中,方法包括向所述对象2次、3次、4次、5次、6次、7次、8次、9次、10次或更多次施用抗体、抗原结合片段或组合物。

[0167] 在某些实施方案中,方法包括向对象多次施用抗体、抗原结合片段或组合物,其中在第一次施用或先前施用后约6小时、约7小时、约8小时、约9小时、约10小时、约11小时、约12小时、约24小时、约48小时、约74小时、约96小时或更长时间分别进行第二次施用或逐次施用。

[0168] 在某些实施方案中,方法包括在对象被弯曲杆菌感染之前至少一次施用抗体、抗原结合片段或组合物。

[0169] 在任何目前公开的方法中,与施用有效量的抗体、抗原结合片段或组合物之前来自对象的粪便样品相比,在施用后来自所述对象的粪便样品包含增加数量的弯曲杆菌菌落形成单位(CFU)。

[0170] 脂质运载蛋白-2(LCN2)是肠道炎症的标志物,并且与上皮损伤和嗜中性粒细胞浸润有关。在任何目前公开的方法中,与施用有效量的抗体、抗原结合片段或组合物之前来自对象的粪便样品相比,在施用后来自所述对象的粪便样品包含减少量LCN2。可以例如使用抗LCN2抗体并进行ELISA测定来测量LCN2。

[0171] 在任何目前公开的方法中,与施用有效量的抗体、抗原结合片段或组合物之前的对象相比,在施用后,所述对象包含在对象的盲肠中减少量的多形核(PMN)细胞浸润,其中

所述PMN细胞是Gr1⁺CD11b⁺。

[0172] 在任何目前公开的方法中,与施用有效量的抗体、抗原结合片段或组合物之前的对象相比,在施用后,所述对象具有改善的盲肠组织学。可以使用标准的组织学分析和评分技术对组织(例如盲肠)的弯曲杆菌感染的损伤、炎症或其它标记进行评分。

[0173] 在任何目前公开的方法中,在施用后,抗体或抗原结合片段在施用后在对象的盲肠和/或排泄物中存在至少4小时或至少8小时。

[0174] 包含本公开内容的抗体或抗原结合片段的组合物也可以与一种或多种其它治疗剂同时施用、也可以在施用一种或多种其它治疗剂之前或之后施用。此类组合疗法可以包括施用含有本发明的化合物和一种或多种另外的活性剂的单一药物剂量制剂,以及施用包含本公开内容的抗体或抗原结合片段的组合物和在其自身的分开剂量制剂中的每种活性剂。例如,如本文所述的抗体或其抗原结合片段和其它活性剂可以在单一口服剂量组合物如片剂或胶囊中一起施用至患者,或者在分开的口服剂量制剂中施用每种药剂。类似地,如本文所述的抗体或抗原结合片段和其它活性剂可以在单一肠胃外剂量组合物(例如在盐水溶液或其它生理学上可接受的溶液中)中一起施用至对象,或者在分开的肠胃外剂量制剂中施用每种药剂。当使用分开的剂量制剂时,包含抗体或抗原结合片段的组合物和一种或多种另外的活性剂可以基本上同一时间(即同时)施用,或者以单独交错的时间(即依次和以任何顺序)施用;组合治疗应理解为包括所有这些方案。

[0175] 在相关方面,提供了目前公开的的抗体、抗原结合片段和组合物的用途。

[0176] 在某些实施方案中,提供了抗体、抗原结合片段或组合物,其用于以下的方法中:(a) 治疗对象中的弯曲杆菌感染;(b) 减轻具有弯曲杆菌感染的对象中的肠道炎症;和/或(c) 增加具有弯曲杆菌感染的对象中的弯曲杆菌的肠道脱落。应理解,治疗、减轻炎症和增加肠脱落如本文所述。

[0177] 在某些实施方案中,提供了抗体、抗原结合片段或组合物,其用于制造或制备药物的方法的用途中,所述药物用于:(a) 治疗对象中的弯曲杆菌感染;(b) 减轻具有弯曲杆菌感染的对象中的肠道炎症;和/或(c) 增加具有弯曲杆菌感染的对象中的弯曲杆菌的肠道脱落。在某些实施方案中,所述药物被配制用于口服施用。

实施例

[0178] 实施例1

[0179] 实验方法

[0180] 分离了针对与细菌运动性、粘附或粘膜侵袭有关的选择的弯曲杆菌抗原的免疫球蛋白,并在体外和离体测试其效力、选择性和广度。通过共转染在哺乳动物细胞中表达相应的重组SIgA(rSIgA),并使用亲和柱层析纯化。

[0181] rSIgA抑制弯曲杆菌运动性的能力通过运动性测定在体外评估(Riazi等人,PLoS One 2013),然而rSIgA与鼠微生物群的广度和交叉反应性通过将mAb与感染的或模拟感染的小鼠的粪便孵育,然后进行人IgA包被的细菌的FACS分析来评价。

[0182] 在C57BL/6小鼠模型中测试口服施用的rSIgA对弯曲杆菌感染的预防活性。在第一个实验中,在mAb施用前48小时,将C57/BL6小鼠用万古霉素通过口服灌胃预处理3次。然后,1小时后,用10⁹CFU的空肠弯曲杆菌菌株81-176(收集号ATCC BAA-2151)感染动物,然后以6

小时的间隔再次施用抗体两次。在另一个实验中,在mAb施用之前48h,24h和12h,用200 μ l PBS中的10mg万古霉素(Sigma-Aldrich)预处理C57BL/6雌性小鼠(21日龄)。然后在用 10^8 CFU的空肠弯曲杆菌81-176(收集号ATCC BAA-2151)通过口服灌胃感染之前2小时,小鼠接受在200 μ l PBS中的200 μ g FliD反应性mAb的单次口服施用。这种感染也可以用其它弯曲杆菌物种进行,例如大肠弯曲杆菌菌株10092/ATB(收集号NCTC 11437)。在整个实验中监测动物粪便中的细菌脱落。通过ELISA测量粪便样品中的肠道炎症的标志物脂质运载蛋白-2,并对盲肠进行组织学评价以研究细菌侵入和粘膜上皮的变化。

[0183] 实施例2

[0184] 弯曲杆菌特异性单克隆IgA抗体的产生

[0185] 迄今为止,尚未将弯曲杆菌鞭毛加帽蛋白(FliD)评估为治疗性单克隆抗体的潜在靶标。选择FliD作为mAb开发的抗原。使用抗原特异性记忆B细胞库分析(AMBRA)(Pinna等人, *Eur. J. Immunol.*, 39:1260-1270(2009)),评价50个瑞士人来源的扁桃体样品中IgG⁺和IgA⁺FliD反应性记忆B细胞的频率(图13)。然后将来自所选扁桃体的IgG⁺和IgA⁺记忆B细胞永生(Traggiai等人, *Nat. Med.*, 10:871-875(2004)),以及使用基于384孔板的高通量平台筛选培养上清液以鉴定表达FliD反应性抗体的细胞克隆。

[0186] 分离产生人单克隆抗体“CAA”和“CCG4”的记忆B细胞克隆,并基于它们对FliD抗原的特异性和亲和力进行选择。CAA1被分离为具有21个氨基酸的HCDR3和V_K1-39/J_K5的由V_H3-48/D2-15/J_H3编码的IgA1。CCG4被分离为带有较短(11个氨基酸)HCDR3和V_L3-27/J_L3的由V_H3-9/D1-7/J_H1编码的IgG3。表1中提供了来自示例性mAb的可变区的核酸和氨基酸序列。

[0187] 人类存在两种IgA同种型亚类,它们主要在铰链区的长度和糖基化方面不同。IgA1具有比IgA2长13个氨基酸的铰链,并且在丝氨酸和苏氨酸残基处含有多达5个O-连接的聚糖。认为IgA1的较长铰链赋予更大的柔性和更长的Fab范围,但也可能有助于IgA1对IgA1蛋白酶的敏感性。IgA2具有较短的铰链区,其缺少脯氨酸-丝氨酸和/或脯氨酸-苏氨酸肽键并且对IgA1蛋白酶具有抗性(Plaut, *Annu. Rev. Microbiol.*, 37:603-622(1983))。此外,IgA2同种型可以通过接触PPs M细胞表面上的Dectin-1受体而经历反向转胞吞作用(reverse transcytosis)(Rochereau等人, *PLoS Biol.*, 11:e1001658(2013))。认为IgG、IgM和IgA1同种型不具有这种能力。认为IgA2的Ca1区和糖基化模式对于与Dectin-1受体的相互作用是重要的,这可以加强针对病原体的适应性免疫(Rochereau等人, *Eur. J. Immunol.*, 45:773-779(2015))。

[0188] 最初相对于IgA1选择IgA2支架用于进一步研究,并且在进一步体外表征之前,CAA1和CCG4均作为rSIgA2产生。对于与抗原不反应的对照抗体,靶向HIV糖蛋白的HGN194 mAb(Corti等人, *PLoS One*, 5:e8805(2010))也表达为rSIgA2。抗体通过质粒共转染在哺乳动物细胞中表达为rSIgA2,并使用CaptureSelect IgA亲和柱进行纯化。

[0189] 使用ELISA和UPLC分析进行纯化的rSIgA的结构和功能表征。弯曲杆菌反应性rSIgA能够识别和结合与严重感染相关的最常见的弯曲杆菌物种,包括最近的临床分离物(图1),显示出与鼠微生物群的有限交叉反应性,这可能是由于与共生物种鞭毛中类似抗原的适度水平的同源或非Fab介导的相互作用。

[0190] 表1提供了根据本公开内容的示例性抗FliD mAb的序列以及示例性FliD蛋白的序列。抗体CDR序列(氨基酸和核苷酸)以粗体显示。体细胞突变产生的抗体残基用下划线标

出。

[0191] 表1序列

[0192]

序列描述	SEQ ID NO.	序列
CAA1 (VH, 针对IgA2m2密码子优化的)	1	gaagcacagctggtggagagcggcggcgccctgatcc agccaggcggctctctgagactgagctgtgaggcctctg gcttcagcctgagctcccacgagatgaactgggtgagac aggcacctggcaagggactggagtggctgagctacatct ccacctctggcatcacaatctactatgcagactccgtgcg gggccggttcaccatcagcagggatacagccaagaact ccctgtacctgcagatgaattctctgaggccgaggacac cgccctgtatcactgtgcccgcatctggcggtactctgc tctggcggcctgtgctatcctcgcggcgcctggacctgt ggggacaggggaaccacagtgacctgtctagcg

序列描述	SEQ ID NO.	序列
CAA1 (VH)	2	EAQLVESGGGLI <u>Q</u> PGGSLRLSCE <u>A</u> SG FSLSSHEMNWVRQAPGKGLEWLSYI STSGITIIYYADSVRGRFTISRDTAKNS LYLQMNSLRAEDTALYHCARDLGG YCSGGLCYPRGALDLWGQGTITVTV SS
CAA1 (VK, 密码子优化的)	3	gacatcctgatgacacagtcctctagctccctgtctgctct gtggcgatagggtagcatcacatgccgcctcccag acaatccggacctacgtgaactggtatcagcagaagccc ggcgagacacctaggctgctgatctacgcagcaaccatc ctgcagcggggcgtgccatccagattctccggctctggc agcggcacagactttaccctgacaatcacctctctgcagc ccgaggatttcggcacctactattgtcagcagaattataag acattcctgacctttggccagggcaccggctggagatca agc
CAA1 (VK)	4	DILMTQSPSSLSASVGDRTITCRASQ TIRTYVNWYQQKPGETPRLLIYAATI LQRGVPSRFSGSGSGTDFTLTITSLQP EDFGTYYCQQNYKTFLTFGQGRLE IK
CAA1 (VH, 天然的)	5	GAGGCGCAGCTGGTGGAGTCTGGG GGAGGCCTGATACAGCCTGGAGGG TCCCTGAGACTCTCCTGTGAAGCCT CTGGCTTCTCCCTCAGTTCTCATG AAATGAATTGGGTCCGCCAGGCTC CAGGGAAGGGGCTGGAGTGGCTTT CATATATTAGTACTAGTGGTATTA CAATATATTACGCGGACTCTGTGA GGGGCCGATTCACCATCTCCAGAG ACACCGCCAAGAAGCTCACTGTATCT GCAAATGAACAGCCTGAGAGCCGA GGACACGGCTCTTTATCACTGTGCG AGAGATCTTGGCGGTATTGTAG TGGTGGTTTGTGCTACCCGAGGG GTGCCTTGGATCTCTGGGGCCAAG GGACAACGGTCACCGTCTCGTCAG
CAA1 (VK, 天然的)	6	GACATCCTGATGACCCAGTCTCCAT CCTCCCTGTCTGCATCTGTGCGGAGA CAGAGTCACCATCACTTGCCGGGC AAGTCAGACCATTTCGCACCTATGT AAATTGGTATCAGCAGAAGCCAGG GGAAACCCCAAGACTCCTTATCTAT GCTGCAACCATTTTGCAGAGAGGG GTCCCATCAAGTTCAGTGGCAGTG GATCTGGGACAGATTTCACTCTCAC CATTACCAGTCTGCAACCTGAAGAT TTTGGAACTTACTACTGTCAACAGA ACTACAAAACCTTTCTCACCTTCG

[0193]

[0194]

序列描述	SEQ ID NO.	序列
		GCCAAGGGACACGACTGGAGATTA AAG
CAA1 (VH, 针对IgA1骨架 密码子优化的)	7	GAAGCACAGCTGGTGGAGAGCGGC GGCGCCTGATCCAGCCAGGCGGC TCTCTGAGACTGAGCTGTGAGGCAT CTGGCTTCAGCCTGAGCTCCCACGA GATGAACTGGGTGAGACAGGCACC TGGCAAGGGCCTGGAGTGGCTGAG CTACATCTCCACCTCTGGCATCACA ATCTACTATGCAGACTCCGTGCGGG GCCGTTTACCATCAGCAGGGATA CAGCCAAGAACTCCCTGTACCTGCA GATGAATTCTCTGAGGGCCGAGGA CACCGCCCTGTATCACTGTGCCCGC GATCTGGGCGGCTACTGCAGCGGC GGCCTGTGCTATCCTCGCGGCGCCC TGGACCTGTGGGGACAGGGAACCA CAGTGACCGTGTCTAGCGCCTCCCC AACATCTCCCAAGGTGTTCCCCCTG AGCCTGTGCTCCACACAGCCTGATG GCAACGTGGTCATCGCCTGTCTGGT GCAGGGCTTCTTTCCTCAGGAGCCA CTGTCTGTGACATGGTCTGAGTCTG GACAGGGAGTGACAGCACGGAATT TCCCCCTTCCCAGGACGCCTCTGG CGATCTGTAT
CAA1 (VH, 针对IgG1骨架 密码子优化的)	8	GAGGCCAGCTGGTGGAAAGCGGC GGCGCCTGATTCAGCCCGGCGGC TCTCTGAGACTGAGCTGTGAGGCAT CTGGCTTCTCCCTGAGCTCCCACGA GATGAACTGGGTGAGACAGGCACC TGGCAAGGGCCTGGAGTGGCTGTC CTACATCTCCACCTCTGGCATCACA ATCTACTATGCCGACTCTGTGCGGG GCCGTTTACCATCTCCAGGGATAC AGCCAAGAACTCTCTGTACCTGCAG ATGAATAGCCTGAGGGCCGAGGAC ACCGCCCTGTATCACTGTGCACGCG ATCTGGGCGGCTACTGCAGCGGCG GCCTGTGCTATCCAAGAGGCGCCCT GGACCTGTGGGGACAGGGAACCAC AGTGACAGTGTCTAGC
CAA1 (HCDR1)	9	G<u>F</u>S<u>L</u>S<u>S</u>H<u>E</u>
CAA1 (HCDR2)	10	I<u>S</u>T<u>S</u>G<u>I</u>T<u>I</u>
CAA1 (HCDR3)	11	A<u>R</u>D<u>L</u>G<u>G</u>Y<u>C</u>S<u>G</u>G<u>L</u>C<u>Y</u>P<u>R</u>G<u>A</u>L<u>D</u>L

[0195]

序列描述	SEQ ID NO.	序列
CAA1 (LCDR1)	12	QTIRTY
CAA1 (LCDR2)	13	AAT
CAA1 (LCDR3)	14	QQNYKTELT
CAA1 (HCDR1; 天然的)	15	GGCTTCTCCCTCAGTTCTCATGAA
CAA1 (HCDR2; 天然的)	16	ATTAGTACTAGTGGTATTACAATA
CAA1 (HCDR3; 天然的)	17	GCGAGAGATCTTGGCGGTTATTGTA GTGGTGGTTTGTGCTACCCGAGGGG TGCCTTGGATCTC
CAA1 (LCDR1; 天然的)	18	CAGACCATTTCGCACCTAT
CAA1 (LCDR2; 天然的)	19	GCTGCAACC
CAA1 (LCDR3; 天然的)	20	CAACAGAACTACAAAACCTTTCTCA CC
CCG4 (VH, 天然的)	21	GAAGTGCAGCTGGTGGAGTCTGGG GGAGGCTTGGTACAGCCTGGCAGG TCCCTGAGACTCTCCTGCGCAGCCT CTGGAATCACCTTTGATGAATATG CCATGTACTGGGTCCGGCAAGCTC CAGGGAAGGGCCTGGAGTGGGTCT CAGGTATTAGTTGGAACAGTGCT AATATAGGCTATGCGGACTCTGTG AAGGGCCGATTACCATCTCCAGA GACAACGCCAAGAAGTCCCTCTAT CTGCAAATGAATAGTCTGAGAGCT GAAGACACGGCCTTGTATTACTGTT CAGGTATAACTGGGACTACGGGG ATACAGTACTGGGGCCAGGGAACC CTGGTCACCGTCTCCTCAG
CCG4 (VH)	22	EVQLVESGGGLVQPGRSLRLSCAAS GITFDEY AMYWVRQAPGKGLEWVS GISWNSANIGYADSVKGRFTISRDN KSLYLQMNSLRAEDTALYYCS SGIT GTTGIQY WGQGLTVTVSS
CCG4 (VL, 天然的)	23	TCCTATGAGCTGACACAGCCATCCT CAGTGTCAAGTGTCTCCGGGACAGA CAGCCAGGATCACCTGCTCAGGAG

[0196]

序列描述	SEQ ID NO.	序列
		ATGTATTGGCAAATACATATGCTC GGTGGTTCCAGCAGAAGCCAGGCC AGGCCCTGTACTGGTGATTTATAA AGACAGT GAGCGGCCCTCAGGGAT CCCTGAGCGATTCTCCGGCTCCAGC TCAGGGACCACAGTCACCTTGATCA TCAGGGGGGCCAGGTTGAGGATG AGGCTGACTATTACTGTTACTCTG CGGCTGACAACAATCGGAGGGTG TTCGGCGGAGGGACCAAGCTGACC GTCCTAG
CCG4 (VL)	24	SYELTQPSSVSVSPGQTARITCSGDVL ANTY ARWFQQKPGQAPVLVIY KDSE RPSGIPERFSGSSSGTTVTLIIRGAQVE DEADYYCYSAADNRRRVFGGGTKL TVL
CCG4 (HCDR1)	25	GITFDEYA
CCG4 (HCDR2)	26	ISWNSANI
CCG4 (HCDR3)	27	SGITGTTGIQY
CCG4 (LCDR1)	28	VLANTY
CCG4 (LCDR2)	29	KDS
CCG4 (LCDR3)	30	YSAADNRRV
CCG4 (HCDR1; 天然的)	31	GGAATCACCTTTGATGAATATGC C
CCG4 (HCDR2; 天然的)	32	ATTAGTTGGAACAGTGCTAATAT A
CCG4 (HCDR3; 天然的)	33	TCAGGTATAACTGGGACTACGGG GATACAGTAC
CCG4 (LCDR1; 天然的)	34	GTATTGGCAAATACATAT
CCG4 (LCDR2; 天然的)	35	AAAGACAGT
CCG4	36	TACTCTGCGGCTGACAACAATCG GAGGGTG

序列描述	SEQ ID NO.	序列
(LCDR3; 天然的)		
CCG4 (VH, 针对IgA2M2骨架密码子优化的)	37	gagggtgcagctggtggaaagcggcggcgccctggtgc agccaggccggctctctgagactgtcttgagcagcatctgg aatcaccttcgacgagtatgcaatgtattgggtgcggcag gcaccaggcaaggactggagtgggtgtccggcatctct tggaacagcgcgaatcggctacgccactccgtgaag ggcaggtttacaatctcccgataacgccaagaagtctc tgtatctgcagatgaatagcctgagggccaggataaccg cctgtactattgtctggcatcacaggcaccacaggcat ccagtactggggccaggccaccctgggtgacagtgagct ccgctcccaacctctccaagggtgtccccctgagcct ggactccacacctcaggatggcaacgtgggtggcctg tctgggtgcagggtcttctcagggccactgagcgtg acctggtctgagagcggccagaacgtgacagcccggaa tttccccctctcaggacgccagcggcgatctgtatacc
CCG4 (VH, 针对IgG1骨架密码子优化的)	38	gagggtgcagctggtggaaagcggcggcgccctggtgc agcctggccggagcctgagactgtcttgagcagcatctgg aatcaccttcgacgagtacgccatgtattgggtgcggcag gcacctggcaaggccctggagtgggtgtctggcatcagc tggaaactccgcaatcggctacgccactctgtgaagg gcaggtttacaatctctcgcgataacgccaagaagcct gtatctgcagatgaattccctgagggccaggataaccgc cctgtactattgtagcggcatcacaggcaccacaggcatc cagtactggggccaggccaccctgggtgacagtgagctc c
CCG4 (VL, 密码子优化的)	39	agctacgagctgaccagcctagctccgtgtctgtgagcc ctggacagacagcaagaatcacatgctctggcgacgtgc tggccaacacatacggcagggtggttcagcagaagcctg gacaggccccctgtctggtcatctacaaggattccgaga ggccatctggcattcctgagcgggtcagcggctctagctc cggcaccacagtgaccctgatcattagaggcggcccagggt ggaggatgaggcagattactattgtatagcggccggac aacaatcggagagtgtcggcggcgaaccaagctgac agtgtctg
IgA1-重链恒定区	40	asptspkvfplslcstqpdgnvviaclvqgffpqpelstv wsesgqgvtnarnfppsqdasgdlytssqtltpatqclag ksvtchvkhytnpsqdvtpcpvpstppspstppstpp spscchprlslhrpaledlllgseantctltglrdasgvft wtpssgksavqgpperdlcgcysvssvlpqcaepwnh gkftfctaaypeskptlatlsksngntfrpevhllpppseel alnelvltclargfspkdvlvrwlqgsqelprekytwa srqepsqgttffavtsilrvaedwkkgdtfscmvghea lplafqtidrlagkpthvnsvvmaevdgtcy
IgA2(m1)-重链恒定区	41	asptspkvfplsldstpqdgnvvviaclvqgffpqpelstv twesgqnvtnarnfppsqdasgdlytssqtltpatqcpd gksvtchvkhytnpsqdvtpcpvpppppcchprlsl hrpaledlllgseantctltglrdasgatftwtpssgksav qgpperdlcgcysvssvlpqcaqpwnhgetftctaahp elktpitanitksngntfrpevhllpppseelalnelvltcla

[0197]

序列描述	SEQ ID NO.	序列
		rgfspkdvlvrvlqgsqelprekyltwasrqepsqgtttf avtsilrvaaedwkkgetfscmvghealplafqtidrl agkpthvnsvvmaevdgty
IgA2(m2)-重链恒定区	42	asptspkvfplslstpdqgnvvvaclvqgffpqpelsv twesegqnvtnarnfpqsqdasgdlytssqtlpatqcpd gksvtchvkhytnssqdvtpcrvpppppcchprlslh rpaledlllgseanltctltglrdasgatfwtppsgksavq gpperdlcgycsvssvlpqcaqpwnhgetftctaahpe lktpltanitksgntfrpevhllpppseelalnelvtlclar gfspkdvlvrvlqgsqelprekyltwasrqepsqgttty avtsilrvaaedwkkgetfscmvghealplafqtidrl magkpthinvsvmaeadgty
空肠弯曲杆菌亚种空肠血清型O:23/36(菌株81-176)鞭毛钩相关蛋白2(Uniprot A0A0H3PIU8)	43	mafgsllslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktllsf qtavsslada tvfakrkvvq sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskgla ndsgfinanl tgttdlffs ngkeyvtvd knntyrelad kineasggei vakivntgek gtpyrllts ketgedsais fyagkkdsng kytsdseae ifknlgweld ttssidpakt kkgygikdas lhiqtaqnae fildgikmfr ssntvtdlgv gmltlntktg einfdvqqdf egvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnssirsi ladlfdsqvv dgttedangn kvntkvmlsm qdfglsnda gtsfdsskf eqkvedpds tesffsnitk yedinhtgev ikqgslnqyl dssgtgnkgl dfkpgdfiv fnnqtdlslk nsdgtmfklt gkteeellqn lanhinskgi eglkvkvesy dqngvkgfkl nfgsdgssdf sikgnatilk elglsdvnit skpiegkgif sklkatlqem tgkdgsitky desltnniks lntskdstqa midrydtma nqwlqyesil nklnqqlnv tnminaanns nn
空肠弯曲杆菌亚种空肠血清型O:2(菌株ATCC 700819 / NCTC 11168)(Uniprot Q9PHW6)	44	mafgsllslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktllsf qtavsslada tvfakrkvvq sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskgla ndggfvnaql ngtadlffs ngkeyvtvd knntyrdlad kineasggei vakivntgek gtpyrllts ketgedsais fyagkkdsng kyqkdinaek ifddlwgld vsasidpakt kkgygikdas lhiqtaqnae fildgikmfr ssntvtdlgv gmltlntktg einfdvqqdf egvtkamqdl vdayndlvtn lnmaatdynse tgtkgtlqgi sevnssirsi ladlfdsqvv dgttedangn kvntkvmlsm qdfglsnda gtsfdsskf eqkvedpds tesffsnitk yedinhtgev iktgslskyl nsngntngl efkpgdfiv fnnqtdlslk nsdgtmfklt gkteeellqn lanhinskgi eglkvkvesy nqnnvtgfrl

[0198]

[0199]

序列描述	SEQ ID NO.	序列
		nfsdgdgssdf sikgdanilk elglsdvnit skpiegkgif sklkatlqem tgkdgsitky deslndiks lntskdstqa midtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
鞭毛钩相关蛋白2 [空 肠弯曲杆菌亚种空肠 NCTC 11168 = ATCC 700819] NCBI参照序列: YP_002343979.1	45	mafslsslsg fgsgvltqdt idklkeaeqk aridpytkki eentkqkdl teiktllsf qtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskgla ndggfvnaql ngtadlffs ngkeyvtvd knntyrldad kineasgei vakivntgek gtpyrllts ketgedsais fyagkkdsng kyqkdinaek ifddlwgld vsasidpdkd kkgygikdas lhiqtaqnae flldgikmfr ssntvdlgv gmtltnktg einfvqqdf egvtkamqdl vdayndlvtn lnaatdyne tgtkgtlqgi sevnssirssi ladlfdsqvv dgttedangn kvntkvmlsm qdfglslnda gtlfdsskf eqkvkedpds tesffsnitk yedinhtgev iktgslskyl nsnggntngl efkpgdfiv fnnqtydlsk nsdgtnfklt gkteellqn lanhinskgi eglkvkesy nqnnvtgfrl nfsdgdgssdf sikgdanilk elglsdvnit skpiegkgif sklkatlqem tgkdgsitky deslndiks lntskdstqa midtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
鞭毛丝加帽蛋白 FliD [空肠弯曲杆菌] NCBI参照序列: WP_038400380.1	46	mafslsslsg fgsgvltqdt idklkeaeqk aridpytkki eentkqkdl teiktllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqsqglandsgfinanl agttdlffs ngkeyvtvd knntyrldad kineasgei vakivntgekgtpyrllts ketgedsais fyagkkdaqg qyksdleak ifkslgweld ttssidpakdkkgygikdas lhiqtaqnae flldgikmfr ssntvdlgv gmtltnktg einfvqqdfegvtkamqdl vdayndlvtn lnaatdyne tgtkgtlqgi sevnssirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlfdsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnggntngl afkpgdfiv fnnqtydlsk nsdgtnfkltgkteellqn lanhinskgi eglkvkesy nqnnvtgfrl nfsdgdgssdf sikgdgsilkelglsdvnit skpiegkgif sklkatlqem tgkdgsitky deslndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
鞭毛钩相关蛋白FliD [空肠弯曲杆菌亚种 空肠81-176]	47	mafslsslsg fgsgvltqdt idklkeaeqk aridpytkki eentkqkdl teiktllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandsgfinanl

序列描述	SEQ ID NO.	序列
GenBank: EAQ73028.1		tgttdltffs ngkeyvtvd knttyrelad kineasgei vakivntgekgtpyrllts ketgedsais fyagkkdsng kytsdseaet ifknlgweld tssidpakdkkgygikdas lhiqtaqnae flldgikmfr ssntvdlgv gmltlntkg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdyse tgtkgtlqgi sevnssirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglsnda gtlfdsskf eqkvkedpds tesffsnitkyedinhtgev ikqgslnqyl dssgtgnkgl dfkpgdftiv fnnqtydlsk nsdgtnfklgtkteellqn lanhinskgi eglkvkvesy dqngvkgfkl nfgdgssdf sikgnatikelglsdvnit skpiegkgif sklkatlqem tgkdsitky desltnniks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
[0200] 鞭毛丝加帽蛋白 FliD [空肠弯曲杆菌] NCBI参照序列: WP_010790846.1	48	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandggfvnaql ngtadltffs ngkeyvtvd knttyrdlad kineasgei vakivntgekgtpyrllts ketgedsais fyagkkdsng kyqkdtnaek ifddlgwgl asasidpakdkkgygikdas lhiqtaqnae flldgikmfr ssntvdlgv gmltlntkg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdyse tgtkgtlqgi sevnssirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglsnda gtlfdsskf eqkvkedpds aesffsnitkyedinhtgei iktgslskyl nsnggntngl dfkpgdftiv fnnqtydlsk nsdgtnfklgtkteellqn lanhinskgi eglkvkvesy dqnnvkgfkl nfgdgssdf sikgdasilkelgldvnit skpiegkgif sklkatlqem tgkdsitky deslndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
多物种: 鞭毛丝加帽 蛋白 FliD [弯曲杆菌] NCBI参照序列: WP_004316510.1	49	mafgslaslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqsqglandggfvnanl ngtadltffs ngkeyvtvd rnttyrdlad kineasgei vakivntgekgtpyrllts ketgedsais fyagkkdang aykndpnaet ifknlgweld atssidlakdkkgygikdts lhiqtaqnae flldgikmfr ssntvdlgv gmltlntkg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdyse tgtkgtlqgi sevnssirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglsnda gtlfdsskf eqkvkedpds

[0201]

序列描述	SEQ ID NO.	序列
		tesffsnitkyedinhtgev iktgslskyl nsnggntngl efkpgdftiv fnnqtydlsk nsdgnfklgtkteellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfgdgsddf sikgdanikelglsdvnit skpiegkgif sklkatlqem tgkdsitky deslndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlstv tnminaans nn
鞭毛丝加帽蛋白 FLiD [空肠弯曲杆菌] NCBI 参照序列: WP_004306838.1	50	mafgslssl fgsgvltqdt idklkeaeqk aridpytkki eentkqkdl teiktllsfqtavsslada tvfakrkvvg sisdnppasl tvnsqvalqs mninvtqlaq kdvyqsqglandggfvnaql ngtadltffs ngkeyvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdaqg qyksdleak ifkslgweld ttssidpakdkkgygikdas lhiqtaqnae ftldgikmfr ssntvdlgv gmtltlntkg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdyse tgtkgtlqgi sevnssirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfgslnda gtlfdsskf ekkvkedpds aesffsnitkyedinhtgev iktgslskyl nsnggsangl dfkpgdftiv fnnqtydlsk nsdgnfklgtkteellqn lanhinskgi eglkvkvesy dqnnvkgfkl nfgdgsddf sikgdanikelglsdvnis skpiegkgif sklkatlqem tgkdsitky deslndiks lntskdstq vmidtrydtma nqwlqyesil nklnqqlntv tnminaans nn
鞭毛丝加帽蛋白 FLiD [空肠弯曲杆菌] NCBI 参照序列: WP_002935293.1	51	mafgslssl fgsgvltqdt idklkeaeqk aridpytkki eentkqkdl teiktllsf qtavsslada tvfakrkvvg sisdnppasl tvnsqvalqs mninvtqlaq kdvyqsqglandsqfvnaql ngtadltffs ngkeyvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdsng kyqkdnaek ifddlgweld vsasidpdkkkgygikdas lhiqtaqnae ftldgikmfr ssntvdlgv gmtltlntkg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdyse tgtkgtlqgi sevnssirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfgslnda gtlfdsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnggntngl efkpgyftiv fnnqtydlsk nsdgnfklgtkteellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfgdgsddf sikgdanikelglsdvnit skpiegkgif sklkatlqem tgkdsitky deslndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaans nn

序列描述	SEQ ID NO.	序列
鞭毛丝加帽蛋白 FliD [空肠弯曲杆菌] NCBI参照序列: WP_002928464.1	52	mafgsllslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandggfvnaql ngtadltffs ngkeyvtvd knttyrdlad kineasggei vakivntgekgtpyrllts ketgedsais fyagkkdsng kyqkdtnaek ifddlwgld asasidpakdkkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtllnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnssirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglsnda gtlndsskf eqkvkedpds aesffsnitkyedinhtgei iktgslskyl nsnggntngl dfkpgdftiv fnnqtydlsk nsdgtmfkltgkteellqn lanhinskgi eglkvkvesy dqnnvkgfkl nfgdgssdf sikgdasilkelglsdvnit skpiegkgif sklkatlqem tgkdgstiky deslndiks lntskdstqamidtrydtma nqwlqyesil nklngqlntv tnminaanns nn
[0202] 鞭毛丝加帽蛋白 FliD [空肠弯曲杆菌] NCBI参照序列: WP_002924910.1	53	mafgsllslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqsqglandggfvnakl ngtadltffs ngkeyvtvd knttyrdlad kineasggei vakivntgekgtpyrllts ketgedsais fyagkkdvqg qyksdseak ifkslgweld ttssidpakdkkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtllnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnssirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglsnda gtlndsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnggntngl efkpgdftiv fnnqtydlsk nsdgtmfkltgkteellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfgdgssdf sikgdanilkelglsdvnit skpiegkgif sklkatlqem tgkdgstiky deslndiks lntskdstqamidtrydtma nqwlqyesil nklngqlntv tnminaanns nn
鞭毛丝加帽蛋白 FliD [空肠弯曲杆菌] NCBI参照序列: WP_002921586.1	54	mafgsllslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandsfinanl tgttdltffs ngkeyvtvd knttyrdlad kineasggei vakivntgekdtpyrllts ketgedsais fyagkkdsng kytsdseae ifknlgweld ttssidpakd kkggygikdas lhiqtaqnae

序列描述	SEQ ID NO.	序列
		flldgikmfr ssntvtdlgv gmtltlnktg einfvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglsnda gtlfdsskf eqkvkedpds tesffsnitkyedinhtgev ikqgslnqyl dssgtgnkgl dfkpgdfiv fnnqtydlsk nsdgtmfklgtkteeellqn lanhinskgi eglkvkvesy dqngvkgfkl nfgdgssdf sikgnatilqelglsdvnit skpiegkgif sklkatlqem tgkdsitky deslndiks lntskdstqamidtrydtma nqwlqyesil nklnqqIntv tnminaanns nn
[0203] 鞭毛丝加帽蛋白 FliD [空肠弯曲杆菌] NCBI参照序列: WP_002908989.1	55	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandggfvnaql ngtadltffs ngkeyvtvtd knntyrdlad kineasgei vakivntgekgtpyrltIs ketgedsais fyagkkdsng kyqkdtnaek ifddlwgld vsasidpdkdkkgygikdas lhiqtaqnae flldgikmfr ssntvtdlgv gmtltlnktg einfvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglsnda gtlfdsskf eqkvkedpds tesffsnitkyedinhtgev ikqgslnqyl dssgtgnkgl dfkpgdfiv fnnqtydlsk nsdgtmfklgtkteeellqn lanhinskgi eglkvkvesy nqnnvtgfkI nfgdgssdf sikgnasilkelglsdvnit skpiegkgif sklkatlqem tgkdsitky deslndiks lntskdstqamidtrydtma nqwlqyesil nklnqqIntv tnminaanns nn
鞭毛丝加帽蛋白 FliD [空肠弯曲杆菌] NCBI参照序列: WP_002901368.1	56	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandsgfinanl tgttdltffs ngkeyvtvtd knntyrdlad kineasgei vakivntgekgtpyrltIs ketgedsais fyagkkdsng kytsdleakt ifknlgweld ttssidpakdkkgygikdas lhiqtaqnae flldgikmfr ssntvtdlgv gmtltlnktg einfvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglsnda gtlfdsskf eqkvkedpds tesffsnitkyedinhtgev ikqgslnqyl dssgtgnkgl dfkpgdfiv fnnqtydlsk nsdgtmfklgtkteeellqn lanhinskgi eglkvkvesy nqnnvtgfri nfgdgssdf

[0204]

序列描述	SEQ ID NO.	序列
		sikgdanilkelglsdvnit skpiegkgif sklkatlqem tkgdgsitky deslndiks lntskdstqamidtrydtma nqwlqyesil nklnqqIntv tnminaanns nn
多物种：鞭毛丝加帽 蛋白 FliD [弯曲杆菌] NCBI 参照序列： WP_002892358.1	57	mafgslsslsg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandggfinanl tgtdlffs ngkeyvtvd knntyrldad kineasgei vakivntgekgtpyrltIs ketgedsais fyagkkdsng aykndpnaet ifknlgweld tttqidpakdkkgygikda shiqtaqna eftldgikmf rrsntvtdlg vgmtltnkt geinfvqqdfegvtkamqd lvdandlvt lnaatdysn etgkgtlqg isevnsirss iladlfdsqvvdgttedang nkvnkvmls mqdfglsld agtIsfdssk feqvkedpd stesffsnitkyedinhtge vikqgslnqy ldssgtgnkg ldfkpgdfti vfnnqtydls knsdgtnfkltgkteeellq nlanhinskg ieglkvkves ydqngvkgfk lnsfgdgssd fsikgnatilqelglsdvnI tskpiegkgi fsklkatlqe mtkgdgsitk ydeslndik slntskdstqamidtrydtm anqwlqyesi lnklnqqIntv tnminaanns snn
鞭毛丝加帽蛋白 FliD [空肠弯曲杆菌] NCBI 参照序列： WP_002874097.1	58	mafgslsslsg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqsqglandggfvnakl ngtadlffs ngkeyvtvd knntyrldad kineasgei vakivntgekgtpyrltIs ketgedsais fyagkkdaqg qyksdseaek ifkslgweld ttssidpakdkkgykysikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltnktg einfvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslda gtlfdsskf eqvkedpds tesffsnitkyedinhtgev iktgslskyl nsnggntngl efkpgdftiv fnnqtydlsk nsdgtnfkltgkteeellqn lanhinskgi eglkvkesy nqnnvtgfrl nfgdgssdf sikgdanilkelglsdvnit skpiegkgif sklkatlqem tkgdgsitky deslndiks lntskdstqamidtrydtma nqwlqyesil nklnqqIntv tnminaanns nn
鞭毛丝加帽蛋白 FliD [空肠弯曲杆菌] NCBI 参照序列：	59	mafgslsslsg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandggfvnaql

序列描述	SEQ ID NO.	序列
WP_002873395.1		ngtadltffs ngkeyvtvtd knntyrdlad kineasggei vakivntgekgtpyrllts ketgedsais fyagkkdsng kyqkdtnaek ifddlwgld vsasidpakdkkgygikdas lhiqtaqnae fldgikmfr ssntvdlgv gmtltnktg einfvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnssirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlfdsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnggntngl efkpgdftiv fnnqtydlsk nsdgtnfklgtkteeellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfgdgssdf sikgdanilkelglsvnit skpiegkgif sklkatlqem tkgdgsitky deslndiks lntskdstqamidtrydtma nqwlqyesil nklnqqIntv tminaanns nn
[0205] 鞭毛钩相关蛋白 FliD [空肠弯曲杆菌亚种 空肠 305] GenBank: EFV08769.1	60	mafgsllslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandggfvnaql ngtadltffs ngkeyvtvtd knntyrdlad kineasggei vakivntgekgtpyrllts ketgedsais fyagkkdsng kyqkdinaek ifddlwgld vsasidpdkdkkgygikdas lhiqtaqnae fldgikmfr ssntvdlgv gmtltnktg einfvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnssirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlfdsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnggntngl efkpgdftiv fnnqtydlsk nsdgtnfklgtkteeellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfgdgssdf sikgdanilkelglsvnit skpiegkgif sklkatlqem tkgdgsitky deslndiks lntskdstqamidtrydtma nqwlqyesil nklnqqIntv tminaanns nn
鞭毛钩相关蛋白 FliD [空肠弯曲杆菌亚种 空肠 327] GenBank: EFV10698.1	61	mafgsllslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandsgfvnanl tgtdltffs ngkeyvtvtd knntyrdlad kineasggei vakivntgekgtpyrllts ketgedsais fyagkkdaqg qyqsdpeaen ifsnlgweld kttqidpakdkkgygikda slhiqtaqna eftldgikmf rsnntvdlg vgmtltnkt geinfvqqdfegvtkamqd lvdavndlvtn lnaatdyns etgtkgtlqg isevnsirss iladlfdsqvvdgttedang nkvnkvmls mqdfglslnd agtlfdssk feqkvkedpd

[0206]

序列描述	SEQ ID NO.	序列
		stesffsnitkyedinhtge vikqgslnqy ldssgtgnkg ldfkpgdfti vfnntydl knsdgtmfklgtkteeellq nlanhinskg ieglkvkves ydqngvkgfk lnfsdgsd fsikgnatilqelglsdvn tskpiegkgi fsklkatlqe mtgkdsitk ydeslndik slntskdstqamidtrydtm anqwlqyesi lnklnqqInt vtnminaann snn
鞭毛钩相关蛋白 FliD [空肠弯曲杆菌亚种 空肠84-25]	62	mafgsllslg fgsgvltqdt idklkeaeqk aridpytkki eentkqkdl teiktllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvqlaq kdvyqsqglandsfinanl agttdltffs ngkeyvtvd knttyrdlad kineasggei vakivntgekgtpyrltIs ketgedsais fyagkkdaqg qyqsdpeaek ifsnlgweld kttqidpakdkkgygikda slhiqtaqna eftldgikmf rsnntvtdlg vgmItlnkt geinfdvqqdfegvtkamqd lvdAyndlvt nlnaatdYns etgkgtlqg isevnsirss iladlfdsqvvdgttedang nkvtkvmls mqdfglsln agtIsfdss feqkvkedpd stesffsnitkyedinhtge viktgsIsky lnsnggntng lefkpgdfti vfnntydl knsdgtmfklgtkteeellq nlanhinskg ieglkvkves ynqnnvtgfr lnfsdgsd fsikgdanilkelglsdvn tskpiegkgi fsklkatlqe mtgkdsitk ydeslndik slntskdstqamidtrydtm anqwlqyesi lnklnqqInt vtnminaann snn
鞭毛钩相关蛋白 FliD [空肠弯曲杆菌亚种 空肠 HB93-13] GenBank: EAQ60315.1	63	mafgsllslg fgsgvltqdt idklkeaeqk aridpytkki eentkqkdl teiktllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvqlaq kdvyqsqglandsfinanl tgttdltffs ngkeyvtvd ksttyrdlad kineasggei vakivntgekgtpyrltIs ketgedsais fyagkkdaqgqyksdseaeki fsnlgweldkttqidp akdkkgygikda slhiqtaqna eftldgikmf rsnntvtdlg vgmItlnkt geinfdvqqdfegvtkamqd lvdAyndlvt nlnaatdYns etgkgtlqg isevnsirss iladlfdsqvvdgttedang nkvtkvmls mqdfglsln agtIsfdss feqkvkedpd stesffsnitkyedinhtge vikqgslnqy ldssgtgnkg lefkpggfti vfnntydl knsdgtmfklgtkteeellq nlanhinskg ieglkvkves ydqngvkgfk lnfsdgsd fsikgdanilkelglsdvn tskpiegkgi fsklkatlqe mtgkdsitk ydeslndik slntskdstqamidtrydtm anqwlqyesi lnklnqqInt vtnminaann snn

序列描述	SEQ ID NO.	序列
鞭毛钩相关蛋白 FliD [空肠弯曲杆菌亚种 空肠 260.94] GenBank: EAQ58732.1	64	mafgsllslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandggfvnaql ngtadltffs ngkeyvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdsng kyqkdtnaek ifddlwgld asasidpakdkkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgittedangn kvntkvmlsm qdfglslna gtlndfsskf eqkvkedpds aesffsnitkyedinhtgei iktgnlskyl nsnggntngl dfkpgdftiv fnnqtydlsk nsdgtnfkltgkteellqn lanhinskgi eglkvkvesy dqnnvkgfkl nfgdgsddf sikgdasilkelglsdvnii skpiegkgif sklkatlqem tkgdgsitky deslndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
[0207] 鞭毛钩相关蛋白 FliD [空肠弯曲杆菌亚种 空肠 CF93-6] GenBank: EAQ57731.1	65	mafgsllslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandggfvnaql ngtadltffs ngkeyvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdsng kyqkdinaek ifddlwgld vsasidpdkdkkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgittedangn kvntkvmlsm qdfglslna gtlndfsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnggntngl efkpgdftiv fnnqtydlsk nsdgtnfkltgkteellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfgdgsddf sikgdanilkelglsdvnit skpiegkgif sklkatlqem tkgdgsitky deslndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
鞭毛钩相关蛋白 FliD [空肠弯曲杆菌 4031] GenBank: CDH62398.1	66	mafgsllslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqsqglandggfvnaki ngtadltffs ngkeyvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdaqg qyksdseak ifkslgweld ttssidpakdkkgygikdas lhiqtaqnae

[0208]

序列描述	SEQ ID NO.	序列
		flldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnssrssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslna agtldsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsngntngl efkpgdftiv fnnqtydlsk nsdgtmfkltgkteeellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfdgdgssdf sikgdanilkelglsdvnit skpiegkgif sklkatlqem tgdgdsitky deslndiks lntskdstqamidtrydtma nqwlqyesil nklnqqIntv tnminaanns nn
鞭毛钩相关蛋白 2 [空 肠弯曲杆菌亚种空肠 M1] GenBank: ADN90737.1	67	mafgslsslq fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandsqfvnanl tgttdltffs ngkeyvtvd knttyrdlad kineasgei vakivntgekgtpyrllts ketgedsais fyagkkdaqg qyqsdpeaen ifsnlgweld kttqidpakdkkgygikda slhiqtaqna eftldgikmf rsnntvtdlg vgmtltlnkt geinfdvqqdfegvtkamqd lvdavndlvtn nlnaatdys etgtkgtlqg isevnsrssi iladlfdsqvvdgttedang nkvnkvmls mqdfglslna agtldsskf fekvkedpd stesffsnitkyedinhtge vikqgslnqy ldssgtgnkg ldfkpgdfti vnnqtydls knsdgtmfkltgkteeellq nlanhinskg ieglvkves ydqngvkgfk lfdgdgssd fsikgnatilqelglsdvnit tskpiegkgi fsklkatlqe mtgkdsitk ydeslndik slntskdstqamidtrydtm anqwlqyesi lnklnqqIntv tnminaanns snn
鞭毛丝加帽蛋白 Flid [空肠弯曲杆菌亚种 空肠菌株 RM3420] GenBank: AOW96893.1	68	mafgslsslq fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandsqfinanl tgttdltffs ngkeyvtvd ksttyrdlad kineasgei vakivntgekgtpyrllts ketgedsais fyagkkdaqg qyksdseak ifsnlgweld kttqidpakdkkgygikda slhiqtaqna eftldgikmf rsnntvtdlg vgmtltlnkt geinfdvqqdfegvtkamqd lvdavndlvtn nlnaatdys etgtkgtlqg isevnsrssi iladlfdsqvvdgttedang nkvnkvmls mqdfglslna agtldsskf fekvkedpd stesffsnitkyedinhtge vikqgslnqy ldssgtgnkg lefkpgdfti vnnqtydls knsdgtmfkltgkteeellq nlanhinskg ieglvkves ydqngvkgfk lfdgdgssd

[0209]

序列描述	SEQ ID NO.	序列
		fsikgdanilkelglsvni tskpiegkgi fsklkatlqe mtgkdsitk ydeslndik slntskdstqamidtrydtm anqwlqyesi lnklnqqlnt vtnminaann snn
鞭毛丝加帽蛋白 FliD [空肠弯曲杆菌亚种 空肠] GenBank: AON66729.1	69	mafgslssl fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqsqglandggfvnaki ngtadlffs ngkeyvtvd knntyrldad kineasgei vakivntgekgtpyrltts ketgedsais fyagkkdaqg qyksdpeak ifkslgweld ttssidpakdkkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgikgtlqgi sevnrsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfgslnda gtlfdsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnggntngl efkpgdftiv fnnqtydlsk nsdgtmfkltgkteellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfgdgsddf sikgdanilkelglsvnit skpiegkgif sklkatlqem tgdgsitky deslndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
鞭毛丝加帽蛋白 FliD [空肠弯曲杆菌亚种 空肠] GenBank: AON65179.1	70	mafgslssl fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqsqglandsgfinanl agttdlffs ngkeyvtvd knntyrldad kineasgei vakivntgekgtpyrltts ketgedsais fyagkkdaqg qyqsdpaeak ifsnlgweld kttqidpakdkkgygikda slhiqtaqna eftldgikmf rsnntvtdlg vgmtltlnkt geinfdvqqdfegvtkamqd lvdayndlvtn nlnaatdys etgkgtlqg isevnsirss iladlfdsqvvdgttedang nkvnkvmls mqdfgslnd agtlfdssk feqkvkedpd stesffsnitkyedinhtge viktgslsky lnsnggntng lafkpgdfti vnnqtydls knsdgtmfkltgkteellq nlanhinskg ieglkvkves ynqnnvtgfr lnsfgdgsdd fsikgdgsilkelglsvni tskpiegkgi fsklkatlqe mtgkdsitk ydeslndik slntskdstqamidtrydtm anqwlqyesi lnklnqqlnt vtnminaann snn
鞭毛丝加帽蛋白[空 肠弯曲杆菌亚种空 肠]	71	mafgslssl fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandggfvnaql

序列描述	SEQ ID NO.	序列
GenBank: AOH51565.1		ngtadltffs ngkeyvtvtd knntyrdlad kineasggei vakivntgekgtpyrllts ketgedsais fyagkkdsng qyqsdseaen ifsnlgweld ktsidpakdkkgygikdas lhiqtaqnae flldgikmfr ssntvdlgv gmtllnktg einfvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkglqgi sevnssirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlfdsskf eqkvkedpds tesffsnitkyedinhtgev intgslskyl npngldfkpg dftivfnnqt ydlsknsdgt nfltkgteellqnlanhi nskgieglkv kvesynqnnv tgrlnfsgd gssdfsikgn atilkelglsdvnitskpie gkgifsklka tlqemtgdg sitkydeslt ndikslntsk dstqamidtrydtmanqwlq yesilnklng qlntvtnmin aannsnn
[0210] 鞭毛丝加帽蛋白FliD [空肠弯曲杆菌亚种 空肠] GenBank: ALF93210.1	72	mafslslsg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvqlaq kdvyqskglandggfvnaql ngtadltffs ngkeyvtvtd knntyrdlad kineasggei vakivntgekgtpyrllts ketgedsais fyagkkdsng kyqkdtnaek ifddlwgld asasidpakdkkgygikdas lhiqtaqnae flldgikmfr ssntvdlgv gmtllnktg einfvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkglqgi sevnssirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlfdsskf eqkvkedpds aesffsnitkyedinhtgei iktgnlskyl nsnggntngl dfkpgdftiv fnnqtydlsk nsdgtfnfltkgteellqn lanhinskgi eglkvvesy dqnnvkgfkl nfgdgssdf sikgdasilkelglsdvni skpiegkgif sklkatlqem tgdgsitky deslndiks lntskdstqamidtrydtma nqwlqyesil nklngqlntv tnminaanns nn
鞭毛钩相关蛋白2 [空 肠弯曲杆菌亚种空 肠] GenBank: AJP35034.1	73	mafslslsg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvqlaq kdvyqsqglandggfvnaql ngtadltffs ngkeyvtvtd knntyrdlad kineasggei vakivntgekgtpyrllts ketgedsais fyagkkdaqg qyesdseak ifkslgweld tssinpakdkkgygikdas lhiqtaqnae flldgikmfr ssntvdlgv gmtllnktg einfvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkglqgi sevnssirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlfdsskf eqkvkedpds

序列描述	SEQ ID NO.	序列
		tesffsnitkyedinhtgev iktgslskyl nsnggntngl efqpgnftiv fnnqtydlsk nsdgtnfkltgkteeellqn lanhinskgi eglkvkvesy dqngvkgfrl nfgdgsddf sikgdanilkdlgsdvnit skpiegkgif skkatlqem tgkdsitky deslndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
鞭毛丝加帽蛋白[空肠弯曲杆菌亚种空肠] GenBank: AOH51565.1	74	mafgsllslg fgsgvltqdt idklkeaeqk aridpytkki eentkqkdl teiktllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvqlaq kdvyqskglandggfvnaql ngtadltffs ngkeyvtvd knntyrldad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdsng qyqsdeaeen ifsnlgweld ktssidpakdkkgygikdas lhiqtaqnae ftldgikmfr ssntvdlgv gmtltlntg einfdvqqdfegvtkamqdl vdayndlvtn lmaatdyse tgtkgtlqgi sevnssirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfgslnda gtlfsdsskf eqkvkedpds tesffsnitkyedinhtgev intgslskyl npngldfpg dfivfnnqt ydlsknsdgt nfkltgkteeellqnlani nskgieglkv kvesynqnnv tgrlnfsgd gssdfsikgn atilkelgsdvnitskpie gkgifsklka tlqemtgdg sitkydeslt ndikslntsk dstqamidtrydtmanqwlq yesilnklnq qlntvtnmin aannsnn
鞭毛加帽蛋白[空肠弯曲杆菌亚种空肠CG8421] GenBank: AHY39787.1	75	mafgsllslg fgsgvltqdt idklkeaeqk aridpytkki eentkqkdl teiktllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvqlaq kdvyqsqglandsfinanl agtadltffs ngkeyvtvd knntyrldad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdaqg qykdleak ifkslgweld ttssidpakdkkgygikdas lhiqtaqnae ftldgikmfr ssntvdlgv gmtltlntg einfdvqqdfegvtkamqdl vdayndlvtn lmaatdyse tgtkgtlqgi sevnssirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfgslnda gtlfsdsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnggntngl afkpgdftiv fnnqtydlsk nsdgtnfkltgkteeellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfgdgsddf sikgdgsilkelgsdvnit skpiegkgif skkatlqem tgkdsitky deslndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn

[0211]

序列描述	SEQ ID NO.	序列
鞭毛加帽蛋白 FliD [空肠弯曲杆菌 32488] GenBank: AGQ95247.1	76	mafgsllslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqsqglandggfvnakl ngtadltffs ngkeyvtvd knttyrdlad kineasggei vakivntgekgtpyrllts ketgedsais fyagkkdvqg qyksdseak ifkslgweld ttssidpakd kkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtllnktg einfdvqqdfegvtkamqdl vdayndlvtn lmaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslna gtlfdsskf eqkvkedpds tesffsnitkyedinhtgev iktgslsky1 nsnggntngl efkpgdftiv fnnqtydlsk nsdgtnfkltgkteellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfgdgssdf sikgdanilkelglsdvnit skpiegkgif sklkatlqem tgkdgstky deslndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
[0212] 鞭毛加帽蛋白[空肠 弯曲杆菌亚种空肠 IA3902] GenBank: ADC28162.1	77	mafgsllslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqsqglandggfvnaql ngtadltffs ngkeyvtvd knttyrdlad kineasggei vakivntgekgtpyrllts ketgedsais fyagkkdsng kyqkdinaek ifddlwgld vsasidpdkkkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtllnktg einfdvqqdfegvtkamqdl vdayndlvtn lmaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslna gtlfdsskf eqkvkedpds tesffsnitkyedinhtgev iktgslsky1 nsnggntngl efkpgdftiv fnnqtydlsk nsdgtnfkltgkteellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfgdgssdf sikgdanilkelglsdvnit skpiegkgif sklkatlqem tgkdgstky deslndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
鞭毛钩相关蛋白 FliD [空肠弯曲杆菌亚种 空肠 81116] GenBank: ABV52108.1	78	mafgsllslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqsqglandsqfvnanl tgttdltffs ngkeyvtvd knttyrdlad kineasggei vakivntgekgtpyrllts ketgedsais fyagkkdaqg qyqsdpaeen ifsnlgweld kttqtidpakkkgygikda slhiqtaqna

序列描述	SEQ ID NO.	序列
		eftldgikmf rsnntvtdlg vgmtltnkt geinfdvqqdfegvtkamqd lvdayndlvt nlnaatdysn etgkgtlqg isevnsirss iladlfdsqvvdgttedang nkvnkvmls mqdfglsln agtlfdsdk feqkvkedpd stesffsnitkyedinhtge vikqgslnqy ldssgtgnkg ldfkpgdfti vfnqtydls knsdgtnfklgtkteeellq nlanhinskg ieglkvkvves ydqngvkgfk lnfsgdgssd fsikgnatilqelglsdvn tskpiegkgi fsklkatlqe mtgkdgsitk ydeslndik slntskdstqamidtrydtm anqwlqyesi lnklnqqln vtminnaann snn
[0213] 鞭毛钩相关蛋白 FliD [空肠弯曲杆菌 RM1221] GenBank: AAW35835.1	79	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandsqfinanl tgttdlffs ngkeyvtvd knntyrldad kineasggei vakivntgekgtpyrltts ketgedsais fyagkkdaqg qyqsdseae ifkslgweld tassidpakd kkgygikdps lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnssirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslna gtlfsdskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nglefkpgd ftivfnqty dlsknsdgn fklgtkteeellqnlanhin skgieglkvk vesynqnnvt gfrlnfsgdg ssdfsikgna silkelglsdvnitkpieg kgifskkat lqemtgdgs itkydesltn dikslntskd sqamidtrydtmanqwlqy esilnknqq lntvtnmina annsnn
鞭毛加帽蛋白 FliD [大肠弯曲杆菌 RM5611] GenBank: AHK75426.1	80	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandsqfinanl tgttdlffs ngkeyvtvd knntyrldad kineasggei vakivntgekgtpyrltts ketgedsais fyagkkdsng qyqsdseae ifsnlgweld ktssidpakdkkgygikdts lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnssirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslna gtlfsdskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsngntngl efkpgdftiv fnnqtydlsk nsdgnfklgtkteeellqn lanhinskgi eglkvkvvesy nqnnvtgfrl nfgsdgssdf sikgnasilkelglsdvnit skpiegkgif

[0214]

序列描述	SEQ ID NO.	序列
		sklkatlqem tgdgsitky deslndiks lntskdstqamidtrydtma nqwlqyesil nklnqqIntv tminaanns nn
鞭毛加帽蛋白 FliD [大肠弯曲杆菌 RM4661] GenBank: AHK76446.1	81	mafgsllslg fgsgvltqdt idklkeaeqk arinpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqn mninvtqlaq kdvyqskglandsgfvnaql ngtadltffs ngkeyvtvd knntyrldad kineasggei vakivntgekgapyrllts ketgedsais fyagkkdssg kytsdsnaet ifknlgweld ttssidpdkdkkgygikdas lhiqtaqnae fildgikmfr ssntvtdlgv gmtltnktg einfvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedvngn kvntkvmlsm qdfglslna gtlfdsskf eqkvkedpds tesffsnitkyedinhtgev intgslskyl npngldfkqg dftivfnnqt ydlsknsdgt nfklgtkteellqnlanhi nsgkieglkv kvesynqngv kgfklfsgd gssdfsikgn asilkelglsdvnitskpie gkgifsklka tlqemtgdg sitkydeslt ndikslntsk dstqamidtr ydtmanqwlq yesilnklnq qlntvtnmin aannssn
鞭毛钩相关蛋白 FliD [大肠弯曲杆菌 15-537360] GenBank: AGZ21001.1	82	mafgsllslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandggfvnaql ngtadltffs ngkeyvtvd knntyrldad kineasggei vakivntgekgtpyrllts ketgedsais fyagkkdsng qyqsdeaeen ifsnlgweld ktssidpakdkkgygikdas lhiqtaqnae fildgikmfr ssntvtdlgv gmtltnktg einfvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslna gtlfdsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnggntngl efkpgdftiv fnnqtydlsk nsdgtnfklgtkteellqn lanhinskgi eglkvvesy nqnnvtgfrl nfsgdgssdf sikgdanikelglsdvnit skpiegkgif sklkatlqem tgdgsitky deslndiks lntskdstqamidtrydtma nqwlqyesil nklnqqIntv tminaanns nn
鞭毛丝加帽蛋白 FliD [大肠弯曲杆菌] NCBI 参照序列: WP_004284951.1	83	mafgsllslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglvndggfvnaql ngtadltffs ngkeyvtvd knntyrldad

序列描述	SEQ ID NO.	序列
		kineasgei vakivntgekgtpyrItls ketgedsais fyagkkdsng kyqkdtnaek ifddlwgld vsasidpakdkkgygikdts lhiqtaqnae flldgikmfr ssntvtdlgv gmltltnktg einfvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnSirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlSfnsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnglefkpg dftivfnnqt ydlsknsdgt nfkltgkteeellqnlani nskgieglkv kvesynqnnv tgrlnfsgd gssdfsikgn asilkelglsdvnitskpie gkgifsklka tlqemtgdg sitkydeslt ndikslntsk dstqamidtr ydtmanqwlq yesilnklng qlntvtnmin aannsnn
[0215] 鞭毛钩相关蛋白2 [大 肠弯曲杆菌] GenBank: AJW57994.1	84	mafgslsslG fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandggfvnaql ngtadltffs ngkeyvtvd knttyrdlad kineasgei vakivntgekgtpyrItls ketgedsais fyagkkdsng kyqkdtnaek ifddlwgld vsasidpakdkkgygikdts lhiqtaqnae flldgikmfr ssntvtdlgv gmltltnktg einfvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnSirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlSfnsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnglefkpg dftivfnnqt ydlsknsdgt nfkltgkteeellqnlani nskgieglkv kvesynqnnv tgrlnfsgd gssdfsikgn asilkelglsdvnitskpie gkgifsklka tlqemtgdg sitkydeslt ndikslntsk dstqamidtrydtmanqwlq yesilnklng qlntvtnmin aannsnn
鞭毛钩相关蛋白2 [大 肠弯曲杆菌] GenBank: ALV00075.1	85	mafgslsslG fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandggfvnaql ngtadltffs ngkeyvtvd knttyrdlad kineasgei vakivntgekgtpyrItls ketgedsais fyagkkdsng kytsdseaet ifknlgweld kttqtidpakdkkgygikda slhiqtaqna eftldgikmf rsnntvtdlg vgmItlnkt geinfvqqdfegvtkamqd lvdAyndlvt nlnaatdyns etgkgtlqg isevnsirss iladlfdsqvvdgttedang nkvnTkvmIs mqdfglslnd agtlSfdssk feqkvkedpd stesffsnitkyedinhtge viktgslsky lnsnglefkp gdfTivfnnq tydlsknsdg tnfkltgkteeellqnlanih inskgieglk

[0216]

序列描述	SEQ ID NO.	序列
		vkvesynqnn vtgfrlnfsg dgssdfsikg nasilkelglsdvnitskpi egkgifsklk atlqemtgd gsitkydeslndikslnskdstqamidtrydtmanqw l qyesilnkn qlntvtnmi naansnn
鞭毛钩相关蛋白FliD [大肠弯曲杆菌 IPSID-1] GenBank: CDL88777.1	86	mafgslssl fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandsgfinanl tgtdlffs ngkeyvtvd knntyrldad kineasgei vakivntgekgtpyrltts ketgedsais fyagkkdsng kysdseaetifknlgweldtssidpakdkkgygikda s lhiqtaqnae fildgikmfr ssntvdlgv gmtltnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdyse tgtkgtlqgi sevnssirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslna gtlfdsskf eqkvkedpds tesffsnitkyedinhtgev ikqgslnqyl dssgtgnkgl dfkpgdfiv fnnqtydlsk nsdgtfnkltgkteellqn lanhinskgi egkvvkvesy dqngvkgfkl nfsdgdssdf sikgnatikelglsdvnit skpiegkgif sklkatlqem tgkdgsitky deslndiks lnskdstqamidtrydtma nqwlyesil nknqqlntv tnminaanns nn
鞭毛钩相关蛋白 2(FliD), 假定的[大肠 弯曲杆菌RM2228] GenBank: EAL57379.1	87	mafgslssl fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandggfvnaql ngtadlffs ngkeyvtvd knntyrldad kineasgei vakivntgekgtpyrltts ketgedsais fyagkkdsng kyqkdtnaek ifddlwgld vsasidpakdkkgygikdts lhiqtaqnae fildgikmfr ssntvdlgv gmtltnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdyse tgtkgtlqgi sevnssirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslna gtlfnsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnglefkpg dfivfnnqt ydlsknsdgt nfkltgkteellqnlanhi nsgieglkv kvesynqnnv tgrlnfsgd gssdfsikgn asilkelglsdvnitskpie gkgifsklka tlqemtgdg sitkydeslt ndikslnsk dstqamidtrydtmanqwlq yesilnknq qlntvtnmin aansnn
鞭毛丝加帽蛋白 FliD [大肠弯曲杆菌] NCBI参照序列:	88	mafgslssl fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandggfvnaql

序列描述	SEQ ID NO.	序列
WP_002842748.1		ngtadltffs ngkeyvtvtd knttyrdlad kineasggei vakivntgekgtpyrllts ketgedsais fyagkkdsng kyqkdtnaek ifddlwgld vsasidpakdkkgygikdts lhiqtaqnae flldgikmfr ssntvtdlgv gmltlntkg einfvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnssirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglsnda gtlfsdsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnglefkpg dftivfnnqt ydlsknsdgt nfkltgkteeellqnlani nskgieglkv kvesynqnnv tgfrlnfsgd gssdfsikgn asilkelglsdvnisskpie gkgifsklka tlqemtgdg sitkydeslt ndikslntsk dstqamidtrydtmanqwlq yesilnklng qlntvtnmin aannsnn
[0217] 鞭毛丝加帽蛋白 FliD [大肠弯曲杆菌] NCBI参照序列: WP_002833936.1	89	mafgslssl gfgsvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandggfvnaql ngtadltffs ngkeyvtvtd knttyrdlad kineasggei vakivntgekgtpyrllts ketgedsais fyagkkdsng qyqsdeaeen ifsnlgweld ktssidpakdkkgygikdas lhiqtaqnae flldgikmfr ssntvtdlgv gmltlntkg einfvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnssirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglsnda gtlfsnsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnglefkpg dftivfnnqt ydlsknsdgt nfkltgkteeellqnlani nskgieglkv kvesynqnnv tgfrlnfsgd gssdfsikgn asilkelglsdvnitskpie gkgifsklka tlqemtgdg sitkydeslt ndikslntsk dstqamidtrydtmanqwlq yesilnklng qlntvtnmin aannsnn
鞭毛钩相关蛋白2 [大 肠弯曲杆菌JV20] GenBank: EFM36457.1	90	mafgslssl gfgsvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglvndggfvnaql ngtadltffs ngkeyvtvtd knttyrdlad kineasggei vakivntgekgtpyrllts ketgedsais fyagkkdsng kyqkdtnaek ifddlwgld vsasidpakdkkgygikdts lhiqtaqnae flldgikmfr ssntvtdlgv gmltlntkg einfvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnssirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglsnda gtlfsnsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnglefkpg dftivfnnqt ydlsknsdgt nfkltgkteeellqnlani

[0218]

序列描述	SEQ ID NO.	序列
		nskgieglkv kvesynqnnv tgrlfnfsgd gssdfsikgn asilkelglsdvnitskpie gkgifsklka tlqemtgdkg sitkydeslt ndikslntsk dstqamidtrydtmanqwlq yesilnklng qlntvtnmin aannsnn
鞭毛丝加帽蛋白 FliD [大肠弯曲杆菌] NCBI参照序列: WP_002832776.1	91	mafslslslg fgsgvltqdt idklkeaeqk aridpytkki eentkqkdl teiktllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandggfvnaql ngtadltffs ngkeyvtvd knttyrdlad kineasgei vakivntgekgtpyrltts ketgedsais fyagkkdsng qyqsdsgaen ifsnlgweld ktssidpakdkkgygikdas lhiqtaqnae fildgikmfr ssntvdlgv gmltlntkg einfvqqdfegvtkamqdl vdayndlvtn lmaatdyse tgtkgtlqgi sevnssirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfgslnda gtlfdsskf eqkvkedpds tesffsnitkyedinhtgev iktgnlskyl nsggntngl efkpgdftiv fnnqtdlslk nsdgtnfklgtkteellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfsgdgssdf sikgdanilkelglsdvnit skpiegkgif sklkatlqem tgkdsitky deslndiks lntskdstqamidtrydtma nqwlqyesil nklngqlntv tnminaanns nn
鞭毛丝加帽蛋白 FliD [大肠弯曲杆菌] NCBI参照序列: WP_002825071.1	92	mafslslslg fgsgvltqdt idklkeaeqk arinpytkki eentkqkdl teiktllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandsfinanl tgtdltffs ngkeyvtvd ksttyrdlad kineasgei vakivntgekgtpyrltts ketgedsais fyagkkdssg kytsdsnaet ifknlgweld ttssidpdkdkkgygikdas lhiqtaqnae fildgikmfr ssntvdlgv gmltlntkg einfvqqdfegvtkamqdl vdayndlvtn lmaatdyse tgtkgtlqgi sevnssirssi ladlfdsqvvdgttedvngn kvntkvmlsm qdfgslnda gtlfdsskf eqkvkedpds tesffsnitkyedinhtgev intgslskyl nsggntngl efkpgdftiv fnnqtdlslk nsdgtnfklgtkteellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfsgdgssdf sikgnasilkelglsdvnit skpiegkgif sklkatlqem tgkdsitky deslndiks lntskdstqamidtrydtma nqwlqyesil nklngqlntv tnminaanns nn
鞭毛丝加帽蛋白 FliD [大肠弯曲杆菌]	93	mafslslslg fgsgvltqdt idklkeaeqk aridpytkki eentkqkdl teiktllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs

序列描述	SEQ ID NO.	序列
NCBI参照序列: WP_002804771.1		mninvtqlaq kdvyqskglandsqfinanl tgttdltffs ngkeyvtvd knntyrdlad kineasgei vakivntgekgtpyrllts ketgedsais fyagkkdsng qyqsdseaen ifsnlgweld ktssidpakdkkgygikdts lhiqtaqnae flldgikmfr ssntvdlgv gmltlntkg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdyse tgtkglqgi sevnssirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlfdsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnggntngl efkpgdftiv fnnqtydlsk nsdgtmfklgtkteellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfgdgssdf sikgnasilkelglsdvnit skpiekgif sklkatlqem tgkdgstiky deslndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
[0219] 鞭毛丝加帽蛋白 FliD [大肠弯曲杆菌] NCBI参照序列: WP_002793506.1	94	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandsqfvnanl tgttdltffs ngkeyvtvd knntyrdlad kineasgei vakivntgekgtpyrllts ketgedsais fyagkkdsng qyqsdseaen ifsnlgweld ktssidpakdkkgygikdts lhiqtaqnae flldgikmfr ssntvdlgv gmltlntkg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdyse tgtkglqgi sevnssirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlfdsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnggntngl efkpgdftiv fnnqtydlsk nsdgtmfklgtkteellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfgdgssdf sikgdasilkelglsdvnis skpiekgif sklkatlqem tgkdgstiky deslndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
鞭毛丝加帽蛋白 FliD [大肠弯曲杆菌] NCBI参照序列: WP_002791831.1	95	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandsqfvsanl tgttdltffs ngkeyvtvd knntyrdlad kineasgei vakivntgekgtpyrllts ketgedsais fyagkkdssg kytsdsnaet ifknlgweld ktssidpakdkkgygikdts lhiqtaqnae flldgikmfr ssntvdlgv gmltlntkg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdyse tgtkglqgi sevnssirssi ladlfdsqvvdgttedangn kvntkvmlsm

序列描述	SEQ ID NO.	序列
[0220]		qdfglsln da gtl sfdsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnggntngl efkpgdftiv fnnqtydlsk nsdgtnfklgtkteeellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfgdgsddf sikgdasilkelglsdvnis skpiegkgif sklkatlqem tgkdgsitky deslndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn

[0221] 实施例3

[0222] rSIgA2形式的弯曲杆菌特异性抗体结合Flid

[0223] 在SIgA2形式中,CAA1和CCG4保持原始的Flid结合活性,对鞭毛蛋白显示出类似的EC50(图7A)。CAA1 SIgA2的EC50为0.02372,CCG4 SIgA2的EC50为0.02954。表位鉴定(epitope binning)显示了一种抗体与抗原的结合不能阻止另一种mAb的结合(图7B),因此表明了两种不同表位的识别。变性还原条件下的蛋白质印迹分析表明两种mAb结合结构上不同的抗原决定簇,其中CAA1靶向线性表位,CCG4是构象表位(图7C)。通过流式细胞术和共聚焦成像证实了抗体对空肠弯曲杆菌和大肠弯曲杆菌历史分离物的鞭毛中的这些表位的可及性(图7D,7E)。

[0224] 实施例4

[0225] rSIgA在体外抑制弯曲杆菌的运动性

[0226] 图2中示意性地示出了运动性测定。结果提供在图3中。CAA1(rSIgA2)与弯曲杆菌鞭毛的结合降低了细菌的运动性,这是使感染和侵袭性最大化所需的条件。针对HIV-1gp120的对照rSIgA2HGN194在运动性测定中不能抑制细菌扩散,表明细菌运动性的抑制不是由SIgA的高度糖基化结构的“先天”交叉反应性引起的。

[0227] 实施例5

[0228] 弯曲杆菌感染的小鼠模型

[0229] 已经提出了特征在于对细菌的炎症反应加剧的基因操作的动物(例如SIGIRR或IL10^{-/-}小鼠)作为研究弯曲杆菌发病机理的模型(Heimesaat等人,Front.Cell.Infect.Microbiol.,4:77(2014);Stahl et al.,PLoS Pathog.,10:e1004264(2014))。然而,这些突变显著改变了鼠免疫系统,以至于即使存在共生微生物也可能潜在地导致自发性小肠结肠炎(Mansfield等人,Infect.Immun.,75:1099-1115(2007))。

[0230] 此外,由于定植抗性和一定水平的耐受性,鼠肠已经显示出对弯曲杆菌的高度抗性,这限制了炎症(Bereswill等人,PLoS One,6:e20953(2011);Chang和Miller,Infect.Immun.,74:5261-5271(2006);Masanta等人,Clin.Dev.Immunol.,2013:526860(2013))。为了克服常驻微生物群的潜在作用,采用了利用万古霉素经口服灌胃进行预处理,弯曲杆菌物种固有地对万古霉素具有抗性(Taylor和Courvalin,Antimicrob.Agents Chemother.,32:1107-1112(1988))。尽管预处理允许盲肠中稳健的细菌定植,但由于观察到最小的炎症迹象,因此其似乎未增强成年野生型小鼠中的病理学(Stahl等人,PLoS Pathog.,10:e1004264(2014))。

[0231] 先前已经报道了与成年动物相比,野生型幼鼠的空肠弯曲杆菌感染的易感性更

高,并且与微生物群组成的显著差异相关(Haag等人, *Eur. J. Microbiol. Immunol. (Bp)*, 2: 2-11 (2012))。为了建立能够在免疫活性条件下重现新生儿和婴幼儿疾病的模型,在幼仔(12日龄)、刚断奶的(21日龄)和成年(56日龄)的C57BL/6小鼠中评价对空肠弯曲杆菌81-176感染的敏感性。在用空肠弯曲杆菌81-176以 10^9 CFU/小鼠感染之前,用万古霉素通过口服灌胃预处理动物以耗损鼠微生物群。在感染后6天来自粪便的弯曲杆菌分离物显示来自21日龄的动物比来自12日龄和56日龄的小鼠有几乎2-1log更高的脱落(图8A)。与这些结果一致,与幼鼠和成年小鼠相比,刚断奶的小鼠显示出显著较高的肠道炎症,如通过粪便中的脂质运载蛋白-2水平和盲肠中的组织学评分值所测量的(图8B-8C)。

[0232] 由于预期抗生素预处理为不同动物的感染提供了相当的小生境,因此其它因素可以解释三组小鼠所显示的对空肠弯曲杆菌感染的不同敏感性。对12日龄、21日龄和56日龄小鼠的粪便中鼠IgA的分析揭示了各组中的不同浓度(图8D)。值得注意的是,与幼鼠和成年小鼠相比,刚断奶小鼠的粪便中呈现可忽略不计的IgA水平。不希望受理论的束缚,这种观察结果可能与奶所提供的母体抗体的外源性供给(12日龄小鼠)和成年动物(56日龄小鼠)中建立的内源性产生的开始之间的转变相一致。因此,刚断奶的小鼠对空肠弯曲杆菌感染的易感性因素可能是由于这些动物中肠道免疫系统的相对不成熟和母体抗体的耗损而导致的分泌型IgA的浓度较低。基于这些数据,选择刚断奶的小鼠作为免疫活性小鼠模型以研究FliD反应性mAb的预防活性。

[0233] CAA1和CCG4与鼠微生物群的脱靶结合可导致mAb可用率降低,因此在预防环境中针对病原体的活性降低。为了研究这一点,评价了rSIgA与刚断奶小鼠的微生物群的潜在交叉反应性。在感染后24小时收集来自经口感染空肠弯曲杆菌、大肠弯曲杆菌或PBS(模拟感染)的动物的粪便,并与两种FliD反应性mAb和对照rSIgA HGN194一起孵育。对来自模拟和感染动物的粪便的人IgA包被的细菌的分析揭示了弯曲杆菌反应性rSIgA能够识别并结合与严重感染有关的最常见物种,显示出与鼠微生物群的有限交叉反应性(图14A)。

[0234] 为了建立用于测试抗体的预防功效的条件,评价了口服施用的SIgA在刚断奶小鼠的不同胃肠道中的药代动力学。与鼠微生物群没有显示出交叉反应性的弯曲杆菌无关的HGN194 rSIgA2(图14A)以在PBS中的 $150\mu\text{g}$ ($\approx 15\text{mg/Kg}$)通过单次口服灌胃施用,并且在施用后2h、4h和8h测量其在不同肠道子区室中的浓度(图14B)。HGN194rSIgA在盲肠中的浓度在施用后的前4小时内保持几乎恒定,然后到8小时趋于显著降低(图14B)。在施用后12小时或24小时检测不到人类抗体(数据未显示)。

[0235] 实施例6

[0236] 口服施用的rSIgA的预防作用

[0237] 将刚断奶的动物(21d)用万古霉素处理,然后在用 10^8 CFU/小鼠的空肠弯曲杆菌81-176口服感染之前两小时,通过单次口服灌胃施用 $200\mu\text{g}$ /小鼠的rSIgA2 CAA1、CCG4、HGN194或PBS。将处理的动物和相应的对照组监测72小时,在此期间记录感染的严重程度和炎症的程度。对来自处理小鼠的粪便的分析揭示了一种趋势,其特征在于在感染后24小时较高的弯曲杆菌脱落,然后随着时间的推移而显著降低。相反地,未处理组和HGN194处理的组在早期的时间点呈现出较低的脱落,然后在感染后48小时呈现出一致的CFU增加(图9A)。图5A和5B显示了来自单独实验的数据,其中在用 10^9 CFU/小鼠的空肠弯曲杆菌81-176感染之前向小鼠施用一次 $200\mu\text{g}$ mAb,以及在用 10^9 CFU/小鼠的空肠弯曲杆菌81-176感染之后向

小鼠施用两次200 μ g mAb。

[0238] 这些结果表明,CAA1和CCG4可以防止或降低病原体粘附到粘膜上皮表面的能力,从而促进在感染后早期通过蠕动或粘膜纤毛(mucocilliary)活性清除细菌。这种假说进一步得到了与对照组(感染的/未处理的和感染的/HGN194处理组)相比,在感染后72小时在CAA1和CCG4处理动物的粪便中记录的显著较低水平的脂质运载蛋白-2(一种与上皮损伤和嗜中性粒细胞浸润有关的肠道炎症标记物)的支持(图9B)。图6显示了来自单独实验的数据,其中在用 10^9 CFU/小鼠的空肠弯曲杆菌81-176感染之前向小鼠施用一次200 μ g mAb,以及用 10^9 CFU/小鼠的空肠弯曲杆菌81-176感染之后向小鼠施用两次200 μ g mAb。

[0239] 在施用较高或较低弯曲杆菌接种物的动物中观察到类似的发现(10^7 或 10^9 CFU/小鼠;图15A,15B)。此外,单次施用Flid反应性mAb处理的动物在盲肠中呈现与未感染的小鼠相当且显著低于HGN194处理组的PMN细胞浸润水平和组织学评分值,因此支持了不受与高度糖基化的SIgA有关的“先天活性”驱动的体内功效(Kaetzel, Immunol. Rev., 206:83-99 (2005); Phalipon et al., Immunity, 17:107-115 (2002)) (图9C,9D)。

[0240] 这些结果表明rSIgA2形式的本公开内容的Flid特异性抗体通过在感染后的早期阶段加速细菌清除来预防口腔递送后的弯曲杆菌感染和炎症。

[0241] 实施例7

[0242] IgA同种型转变不影响CAA1预防活性

[0243] 由于IgA1和IgA2可以在Fab范围、柔韧性和糖基化方面具有可能影响聚合Ig在肠中的交联能力和/或持久性的差异,进行以下实验以确定两种IgA同种型是否可以在本文所述的弯曲杆菌感染的免疫活性小鼠模型中发挥不同的预防活性。

[0244] Flid反应性CAA1重组产生为SIgA1和SIgA2。通过分析方法和通过用来自Neisseria gonorrhoeae的IgA1蛋白酶消化证实了两个亚类的正确组装(图16A)。CAA1 SIgA1和SIgA2显示出与Flid相当的结合(图16B),并且在两种形式之间未观察到在体外与弯曲杆菌物种的反应性或者离体与鼠微生物群的反应性的显著差异(图16C,16D)。

[0245] 然后在弯曲杆菌感染的鼠模型中测试了这两个亚类的预防活性。与先前的发现一致,施用Flid反应性mAb的动物在感染后的早期时间点显示出较高的弯曲杆菌脱落,然后随着时间的推移而减少,而感染的未处理的动物产生相反的趋势(图10A)。尽管CAA1 rSIgA2比rSIgA1更快地加速脱落,但两个亚类同样能够限制感染动物中的炎症,如通过感染后72小时盲肠中的粪便中脂质运载蛋白-2水平、PMN浸润和相应的组织学评分所示(图10B-10D)。

[0246] 这些结果表明,在体内模型中,IgA1和IgA2之间的结构差异不会导致这两种CAA1形式所发挥的预防活性差异。

[0247] 实施例8

[0248] 当以IgG表达时mAb CAA1和CCG4具有降低的口服预防活性

[0249] 尽管认为SIgA是与肠粘膜相关的表达最丰富的抗体,并且可能是抵抗肠道病原体的第一道防线,但它们的特征在于复杂的蛋白质结构以及与基于IgG的单克隆抗体相比,它们作为药物的开发可能存在挑战。由于弯曲杆菌反应性mAb的活性显示出依赖于对Flid的特异性,因此产生了CAA1、CCG4和与弯曲杆菌无关的抗体HGN194作为rIgG1,并评价与其相应的SIgA2对应物相比的预防活性。

[0250] 由于糖基化可能影响mAb与粘膜表面上的粘蛋白相互作用的能力,通过向21日龄小鼠单次口服灌胃施用抗体,然后在2h、4h和8h后测量其在不同肠道子区室中的浓度来评估对照mAb HGN194作为rIgG1在鼠肠道中的定位和持久性(图14C)。与HGN194 rSIgA2一样,在每个时间点,在盲肠中检测到最高浓度的rIgG1;然而,在该肠道子区室中,rIgG1浓度倾向于比rSIgA2降低得更快,在施用后4小时观察到显著减少(图14B,14C)。

[0251] 还评价了Flid反应性mAb CAA1和CCG4作为rIgG1或SIgA2的预防活性。在用空肠弯曲杆菌81-176感染之前2小时,将mAb口服施用至刚断奶的小鼠。有趣的是,尽管用SIgA2抗体处理的动物显示出特征在于感染后24小时出现较高的脱落,然后在48h和72h显著降低的先前观察到的模式,但用相同抗体的IgG形式处理的组显示出类似于未处理组的趋势(图11A和17A)。与它们的聚合对应物相比,CAA1和CCG4 IgG限制炎症的能力降低进一步证实了SIgA形式对体内功效的重要性,如感染后72天感染动物的盲肠中的PMN细胞浸润和粪便中的脂质运载蛋白-2水平所示(图11B,C和17B,17C)。总的来说,在用Flid反应性IgG抗体处理的小鼠和未处理的动物之间没有观察到组织学评分的显著差异。相反,SIgA形式的抗体能够重现先前观察到的有益效果,将盲肠中的组织学评分保持为显著低于未处理小鼠和IgG处理的小鼠的值(图11D和17D)。

[0252] 这些数据表明,与表达为SIgA的相同抗体相比,当在弯曲杆菌感染之前口服施用,CAA1和CCG4 IgG具有有限的预防活性。不希望受理论的束缚,口服施用的CAA1和CCG4 IgG的活性的缺乏可能依赖于胃肠道中较低的持久性和与SIgA形式相关的不同交联特性。

[0253] 可以组合上述各种实施方案以提供其它实施方案。在本说明书中提及和/或在申请数据表(包括2018年7月17日提交的美国临时专利申请第62/699,573号)中列出的所有美国专利、美国专利申请公开、美国专利申请、外国专利、外国专利申请和非专利公开通过引用以其整体并入本文。如果需要使用各种专利、申请和出版物的概念来提供另外的实施方案,则可以修改实施方案的方面。

[0254] 可以根据以上详细描述对实施方案进行这些和其它改变。通常,在所附权利要求中,所使用的术语不应被解释为将权利要求限制于说明书和权利要求中所公开的具体实施方案,而应被解释为包括所有可能的实施方案以及这些权利要求所授权的等同物的全部范围。因此,权利要求不受本公开内容的限制。

- [0001] 序列表
- [0002] <110> 胡默波斯生物医学公司(Humabs Biomed SA)
- [0003] 法比奥·格拉西(Grassi, Fabio)
- [0004] 利萨·佩鲁扎(Perruzza, Lisa)
- [0005] 马迪奥·皮祖托(Pizzuto, Matteo)
- [0006] 法比奥·贝尼尼(Benigni, Fabio)
- [0007] 达维德·科尔蒂(Corti, Davide)
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- [0009] <130> 470082.406W0
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- [0263] gggactacgg ggatacagta ctggggccag ggaaccctgg tcaccgtctc ctcag 355
- [0264] <210> 22
- [0265] <211> 118
- [0266] <212> PRT
- [0267] <213> 人工序列(Artificial Sequence)
- [0268] <220>
- [0269] <223> 合成序列-CCG4 (VH)
- [0270] <400> 22
- [0271] Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
- [0272] 1 5 10 15

[0273]	Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Ile Thr Phe Asp Glu Tyr
[0274]	20 25 30
[0275]	Ala Met Tyr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
[0276]	35 40 45
[0277]	Ser Gly Ile Ser Trp Asn Ser Ala Asn Ile Gly Tyr Ala Asp Ser Val
[0278]	50 55 60
[0279]	Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Lys Ser Leu Tyr
[0280]	65 70 75 80
[0281]	Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
[0282]	85 90 95
[0283]	Ser Gly Ile Thr Gly Thr Thr Gly Ile Gln Tyr Trp Gly Gln Gly Thr
[0284]	100 105 110
[0285]	Leu Val Thr Val Ser Ser
[0286]	115
[0287]	<210> 23
[0288]	<211> 322
[0289]	<212> DNA
[0290]	<213> 人工序列(Artificial Sequence)
[0291]	<220>
[0292]	<223> 合成序列-CCG4 (VL,天然的)
[0293]	<400> 23
[0294]	tcctatgagc tgacacagcc atcctcagtg tcagtgtctc cgggacagac agccaggatc 60
[0295]	acctgctcag gagatgtatt ggcaaataca tatgctcggg ggttccagca gaagccaggc 120
[0296]	caggcccctg tactggtgat ttataaagac agtgagcggc cctcagggat ccctgagcga 180
[0297]	ttctccggct ccagctcagg gaccacagtc accttgatca tcaggggggc ccaggttgag 240
[0298]	gatgaggctg actattactg ttactctgcg gctgacaaca atcggagggt gttcggcgga 300
[0299]	gggaccaagc tgaccgtcct ag 322
[0300]	<210> 24
[0301]	<211> 107
[0302]	<212> PRT
[0303]	<213> 人工序列(Artificial Sequence)
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[0305]	<223> 合成序列-CCG4 (VL)
[0306]	<400> 24
[0307]	Ser Tyr Glu Leu Thr Gln Pro Ser Ser Val Ser Val Ser Pro Gly Gln
[0308]	1 5 10 15
[0309]	Thr Ala Arg Ile Thr Cys Ser Gly Asp Val Leu Ala Asn Thr Tyr Ala
[0310]	20 25 30
[0311]	Arg Trp Phe Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr

[0312]	35	40	45
[0313]	Lys Asp Ser Glu Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser		
[0314]	50	55	60
[0315]	Ser Ser Gly Thr Thr Val Thr Leu Ile Ile Arg Gly Ala Gln Val Glu		
[0316]	65	70	75 80
[0317]	Asp Glu Ala Asp Tyr Tyr Cys Tyr Ser Ala Ala Asp Asn Asn Arg Arg		
[0318]	85	90	95
[0319]	Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu		
[0320]	100	105	
[0321]	<210> 25		
[0322]	<211> 8		
[0323]	<212> PRT		
[0324]	<213> 人工序列(Artificial Sequence)		
[0325]	<220>		
[0326]	<223> 合成序列-CCG4 (HCDR1)		
[0327]	<400> 25		
[0328]	Gly Ile Thr Phe Asp Glu Tyr Ala		
[0329]	1	5	
[0330]	<210> 26		
[0331]	<211> 8		
[0332]	<212> PRT		
[0333]	<213> 人工序列(Artificial Sequence)		
[0334]	<220>		
[0335]	<223> 合成序列-CCG4 (HCDR2)		
[0336]	<400> 26		
[0337]	Ile Ser Trp Asn Ser Ala Asn Ile		
[0338]	1	5	
[0339]	<210> 27		
[0340]	<211> 11		
[0341]	<212> PRT		
[0342]	<213> 人工序列(Artificial Sequence)		
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[0344]	<223> 合成序列-CCG4 (HCDR3)		
[0345]	<400> 27		
[0346]	Ser Gly Ile Thr Gly Thr Thr Gly Ile Gln Tyr		
[0347]	1	5	10
[0348]	<210> 28		
[0349]	<211> 6		
[0350]	<212> PRT		

- [0351] <213> 人工序列(Artificial Sequence)
 [0352] <220>
 [0353] <223> 合成序列-CCG4 (LCDR1)
 [0354] <400> 28
 [0355] Val Leu Ala Asn Thr Tyr
 [0356] 1 5
 [0357] <210> 29
 [0358] <211> 3
 [0359] <212> PRT
 [0360] <213> 人工序列(Artificial Sequence)
 [0361] <220>
 [0362] <223> 合成序列-CCG4 (LCDR2)
 [0363] <400> 29
 [0364] Lys Asp Ser
 [0365] 1
 [0366] <210> 30
 [0367] <211> 10
 [0368] <212> PRT
 [0369] <213> 人工序列(Artificial Sequence)
 [0370] <220>
 [0371] <223> 合成序列-CCG4 (LCDR3)
 [0372] <400> 30
 [0373] Tyr Ser Ala Ala Asp Asn Asn Arg Arg Val
 [0374] 1 5 10
 [0375] <210> 31
 [0376] <211> 24
 [0377] <212> DNA
 [0378] <213> 人工序列(Artificial Sequence)
 [0379] <220>
 [0380] <223> 合成序列-CCG4 (HCDR1;天然的)
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 [0382] ggaatcacct ttgatgaata tgcc 24
 [0383] <210> 32
 [0384] <211> 24
 [0385] <212> DNA
 [0386] <213> 人工序列(Artificial Sequence)
 [0387] <220>
 [0388] <223> 合成序列-CCG4 (HCDR2;天然的)
 [0389] <400> 32

- [0390] attagttgga acagtgctaa tata 24
[0391] <210> 33
[0392] <211> 33
[0393] <212> DNA
[0394] <213> 人工序列(Artificial Sequence)
[0395] <220>
[0396] <223> 合成序列-CCG4 (HCDR3;天然的)
[0397] <400> 33
[0398] tcaggtataa ctgggactac ggggatacag tac 33
[0399] <210> 34
[0400] <211> 18
[0401] <212> DNA
[0402] <213> 人工序列(Artificial Sequence)
[0403] <220>
[0404] <223> 合成序列-CCG4 (LCDR1;天然的)
[0405] <400> 34
[0406] gtattggcaa atacatat 18
[0407] <210> 35
[0408] <211> 9
[0409] <212> DNA
[0410] <213> 人工序列(Artificial Sequence)
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[0412] <223> 合成序列-CCG4 (LCDR2;天然的)
[0413] <400> 35
[0414] aaagacagt 9
[0415] <210> 36
[0416] <211> 30
[0417] <212> DNA
[0418] <213> 人工序列(Artificial Sequence)
[0419] <220>
[0420] <223> 合成序列-CCG4 (LCDR2;天然的)
[0421] <400> 36
[0422] tactctgcfg ctgacaacaa tcggagggtg 30
[0423] <210> 37
[0424] <211> 549
[0425] <212> DNA
[0426] <213> 人工序列(Artificial Sequence)
[0427] <220>
[0428] <223> 合成序列-CCG4 (VH,针对IgA2M2骨架密码子优化的)

- [0429] <400> 37
- [0430] gaggtgcagc tgggtgaaag cggcggcggc ctggtgcagc caggccggtc tctgagactg 60
- [0431] tcttgtgcag catctggaat caccttcgac gagtatgcaa tgtattgggt gcggcaggca 120
- [0432] ccaggcaagg gactggagtg ggtgtccggc atctcttggga acagcgccaa tatcggctac 180
- [0433] gccgactccg tgaagggcag gtttacaatc tcccgcgata acgccaagaa gtctctgtat 240
- [0434] ctgcagatga atagcctgag ggccgaggat accgccctgt actattgctc tggcatcaca 300
- [0435] ggcaccacag gcatccagta ctggggccag ggcaccctgg tgacagtgag ctccgcctcc 360
- [0436] ccaacctctc ccaaggtggt ccccctgagc ctggactcca cacctcagga tggcaacgtg 420
- [0437] gtggtggcct gtctggtgca gggcttcttt cctcaggagc cactgagcgt gacctggtct 480
- [0438] gagagcggcc agaacgtgac agcccggaat tttccccctt ctcaggacgc cagcggcgat 540
- [0439] ctgtatacc 549
- [0440] <210> 38
- [0441] <211> 354
- [0442] <212> DNA
- [0443] <213> 人工序列(Artificial Sequence)
- [0444] <220>
- [0445] <223> 合成序列-CCG4 (VH,针对IgG1骨架密码子优化的)
- [0446] <400> 38
- [0447] gaggtgcagc tgggtgaaag cggcggcggc ctggtgcagc ctggccggag cctgagactg 60
- [0448] tcttgtgcag catctggaat caccttcgac gagtacgcca tgtattgggt gcggcaggca 120
- [0449] cctggcaagg gcctggagtg ggtgtctggc atcagctgga actccgccaat tatcggctac 180
- [0450] gccgactctg tgaagggcag gtttacaatc tctcgcgata acgccaagaa gagcctgtat 240
- [0451] ctgcagatga attccctgag ggccgaggat accgccctgt actattgtag cggcatcaca 300
- [0452] ggcaccacag gcatccagta ctggggccag ggcaccctgg tgacagtgag ctcc 354
- [0453] <210> 39
- [0454] <211> 321
- [0455] <212> DNA
- [0456] <213> 人工序列(Artificial Sequence)
- [0457] <220>
- [0458] <223> 合成序列-CCG4 (VL,密码子优化的)
- [0459] <400> 39
- [0460] agctacgagc tgaccagacc tagctccgtg tctgtgagcc ctggacagac agcaagaatc 60
- [0461] acatgctctg gcgacgtgct ggccaacaca tacgccaggt ggtttcagca gaagcctgga 120
- [0462] caggcccccg tgctggtcat ctacaaggat tccgagaggc catctggcat tcctgagcgg 180
- [0463] ttcagcggct ctagctccgg caccacagtg accctgatca ttagaggcgc ccaggtggag 240
- [0464] gatgagcagc attactattg ttatagcgcc gccgacaaca atcggagagt gttcggcggc 300
- [0465] ggaaccaagc tgacagtgct g 321
- [0466] <210> 40
- [0467] <211> 353

[0468] <212> PRT
 [0469] <213> 人工序列(Artificial Sequence)
 [0470] <220>
 [0471] <223> 合成序列-IgA1 -重链恒定区
 [0472] <400> 40
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 [0474] 1 5 10 15
 [0475] Gln Pro Asp Gly Asn Val Val Ile Ala Cys Leu Val Gln Gly Phe Phe
 [0476] 20 25 30
 [0477] Pro Gln Glu Pro Leu Ser Val Thr Trp Ser Glu Ser Gly Gln Gly Val
 [0478] 35 40 45
 [0479] Thr Ala Arg Asn Phe Pro Pro Ser Gln Asp Ala Ser Gly Asp Leu Tyr
 [0480] 50 55 60
 [0481] Thr Thr Ser Ser Gln Leu Thr Leu Pro Ala Thr Gln Cys Leu Ala Gly
 [0482] 65 70 75 80
 [0483] Lys Ser Val Thr Cys His Val Lys His Tyr Thr Asn Pro Ser Gln Asp
 [0484] 85 90 95
 [0485] Val Thr Val Pro Cys Pro Val Pro Ser Thr Pro Pro Thr Pro Ser Pro
 [0486] 100 105 110
 [0487] Ser Thr Pro Pro Thr Pro Ser Pro Ser Cys Cys His Pro Arg Leu Ser
 [0488] 115 120 125
 [0489] Leu His Arg Pro Ala Leu Glu Asp Leu Leu Leu Gly Ser Glu Ala Asn
 [0490] 130 135 140
 [0491] Leu Thr Cys Thr Leu Thr Gly Leu Arg Asp Ala Ser Gly Val Thr Phe
 [0492] 145 150 155 160
 [0493] Thr Trp Thr Pro Ser Ser Gly Lys Ser Ala Val Gln Gly Pro Pro Glu
 [0494] 165 170 175
 [0495] Arg Asp Leu Cys Gly Cys Tyr Ser Val Ser Ser Val Leu Pro Gly Cys
 [0496] 180 185 190
 [0497] Ala Glu Pro Trp Asn His Gly Lys Thr Phe Thr Cys Thr Ala Ala Tyr
 [0498] 195 200 205
 [0499] Pro Glu Ser Lys Thr Pro Leu Thr Ala Thr Leu Ser Lys Ser Gly Asn
 [0500] 210 215 220
 [0501] Thr Phe Arg Pro Glu Val His Leu Leu Pro Pro Pro Ser Glu Glu Leu
 [0502] 225 230 235 240
 [0503] Ala Leu Asn Glu Leu Val Thr Leu Thr Cys Leu Ala Arg Gly Phe Ser
 [0504] 245 250 255
 [0505] Pro Lys Asp Val Leu Val Arg Trp Leu Gln Gly Ser Gln Glu Leu Pro
 [0506] 260 265 270

[0507]	Arg Glu Lys Tyr Leu Thr Trp Ala Ser Arg Gln Glu Pro Ser Gln Gly
[0508]	275 280 285
[0509]	Thr Thr Thr Phe Ala Val Thr Ser Ile Leu Arg Val Ala Ala Glu Asp
[0510]	290 295 300
[0511]	Trp Lys Lys Gly Asp Thr Phe Ser Cys Met Val Gly His Glu Ala Leu
[0512]	305 310 315 320
[0513]	Pro Leu Ala Phe Thr Gln Lys Thr Ile Asp Arg Leu Ala Gly Lys Pro
[0514]	325 330 335
[0515]	Thr His Val Asn Val Ser Val Val Met Ala Glu Val Asp Gly Thr Cys
[0516]	340 345 350
[0517]	Tyr
[0518]	<210> 41
[0519]	<211> 340
[0520]	<212> PRT
[0521]	<213> 人工序列(Artificial Sequence)
[0522]	<220>
[0523]	<223> 合成序列-IgA2(m1) -重链恒定区
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[0526]	1 5 10 15
[0527]	Pro Gln Asp Gly Asn Val Val Val Ala Cys Leu Val Gln Gly Phe Phe
[0528]	20 25 30
[0529]	Pro Gln Glu Pro Leu Ser Val Thr Trp Ser Glu Ser Gly Gln Asn Val
[0530]	35 40 45
[0531]	Thr Ala Arg Asn Phe Pro Pro Ser Gln Asp Ala Ser Gly Asp Leu Tyr
[0532]	50 55 60
[0533]	Thr Thr Ser Ser Gln Leu Thr Leu Pro Ala Thr Gln Cys Pro Asp Gly
[0534]	65 70 75 80
[0535]	Lys Ser Val Thr Cys His Val Lys His Tyr Thr Asn Pro Ser Gln Asp
[0536]	85 90 95
[0537]	Val Thr Val Pro Cys Pro Val Pro Pro Pro Pro Pro Cys Cys His Pro
[0538]	100 105 110
[0539]	Arg Leu Ser Leu His Arg Pro Ala Leu Glu Asp Leu Leu Leu Gly Ser
[0540]	115 120 125
[0541]	Glu Ala Asn Leu Thr Cys Thr Leu Thr Gly Leu Arg Asp Ala Ser Gly
[0542]	130 135 140
[0543]	Ala Thr Phe Thr Trp Thr Pro Ser Ser Gly Lys Ser Ala Val Gln Gly
[0544]	145 150 155 160
[0545]	Pro Pro Glu Arg Asp Leu Cys Gly Cys Tyr Ser Val Ser Ser Val Leu

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[0547]	Pro	Gly	Cys	Ala	Gln	Pro	Trp	Asn	His	Gly	Glu	Thr	Phe	Thr	Cys	Thr
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[0549]	Ala	Ala	His	Pro	Glu	Leu	Lys	Thr	Pro	Leu	Thr	Ala	Asn	Ile	Thr	Lys
[0550]				195						200					205	
[0551]	Ser	Gly	Asn	Thr	Phe	Arg	Pro	Glu	Val	His	Leu	Leu	Pro	Pro	Pro	Ser
[0552]				210						215					220	
[0553]	Glu	Glu	Leu	Ala	Leu	Asn	Glu	Leu	Val	Thr	Leu	Thr	Cys	Leu	Ala	Arg
[0554]				225						230					235	
[0555]	Gly	Phe	Ser	Pro	Lys	Asp	Val	Leu	Val	Arg	Trp	Leu	Gln	Gly	Ser	Gln
[0556]					245						250					255
[0557]	Glu	Leu	Pro	Arg	Glu	Lys	Tyr	Leu	Thr	Trp	Ala	Ser	Arg	Gln	Glu	Pro
[0558]					260						265					270
[0559]	Ser	Gln	Gly	Thr	Thr	Thr	Phe	Ala	Val	Thr	Ser	Ile	Leu	Arg	Val	Ala
[0560]					275											285
[0561]	Ala	Glu	Asp	Trp	Lys	Lys	Gly	Asp	Thr	Phe	Ser	Cys	Met	Val	Gly	His
[0562]					290											300
[0563]	Glu	Ala	Leu	Pro	Leu	Ala	Phe	Thr	Gln	Lys	Thr	Ile	Asp	Arg	Leu	Ala
[0564]					305											320
[0565]	Gly	Lys	Pro	Thr	His	Val	Asn	Val	Ser	Val	Val	Met	Ala	Glu	Val	Asp
[0566]						325										335
[0567]	Gly	Thr	Cys	Tyr												
[0568]						340										
[0569]	<210>	42														
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[0571]	<212>	PRT														
[0572]	<213>	人工序列(Artificial Sequence)														
[0573]	<220>															
[0574]	<223>	合成序列-IgA2(m2)	-重链恒定区													
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[0577]																
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[0579]	Pro	Gln	Asp	Gly	Asn	Val	Val	Val	Ala	Cys	Leu	Val	Gln	Gly	Phe	Phe
[0580]																
[0581]																
[0582]																
[0583]																
[0584]																
[0584]	Thr	Thr	Ser	Ser	Gln	Leu	Thr	Leu	Pro	Ala	Thr	Gln	Cys	Pro	Asp	Gly

[0585]	65	70	75	80
[0586]	Lys Ser Val Thr Cys His Val Lys His Tyr Thr Asn Ser Ser Gln Asp			
[0587]		85	90	95
[0588]	Val Thr Val Pro Cys Arg Val Pro Pro Pro Pro Pro Cys Cys His Pro			
[0589]		100	105	110
[0590]	Arg Leu Ser Leu His Arg Pro Ala Leu Glu Asp Leu Leu Leu Gly Ser			
[0591]		115	120	125
[0592]	Glu Ala Asn Leu Thr Cys Thr Leu Thr Gly Leu Arg Asp Ala Ser Gly			
[0593]		130	135	140
[0594]	Ala Thr Phe Thr Trp Thr Pro Ser Ser Gly Lys Ser Ala Val Gln Gly			
[0595]		145	150	160
[0596]	Pro Pro Glu Arg Asp Leu Cys Gly Cys Tyr Ser Val Ser Ser Val Leu			
[0597]		165	170	175
[0598]	Pro Gly Cys Ala Gln Pro Trp Asn His Gly Glu Thr Phe Thr Cys Thr			
[0599]		180	185	190
[0600]	Ala Ala His Pro Glu Leu Lys Thr Pro Leu Thr Ala Asn Ile Thr Lys			
[0601]		195	200	205
[0602]	Ser Gly Asn Thr Phe Arg Pro Glu Val His Leu Leu Pro Pro Pro Ser			
[0603]		210	215	220
[0604]	Glu Glu Leu Ala Leu Asn Glu Leu Val Thr Leu Thr Cys Leu Ala Arg			
[0605]		225	230	240
[0606]	Gly Phe Ser Pro Lys Asp Val Leu Val Arg Trp Leu Gln Gly Ser Gln			
[0607]		245	250	255
[0608]	Glu Leu Pro Arg Glu Lys Tyr Leu Thr Trp Ala Ser Arg Gln Glu Pro			
[0609]		260	265	270
[0610]	Ser Gln Gly Thr Thr Thr Tyr Ala Val Thr Ser Ile Leu Arg Val Ala			
[0611]		275	280	285
[0612]	Ala Glu Asp Trp Lys Lys Gly Glu Thr Phe Ser Cys Met Val Gly His			
[0613]		290	295	300
[0614]	Glu Ala Leu Pro Leu Ala Phe Thr Gln Lys Thr Ile Asp Arg Met Ala			
[0615]		305	310	320
[0616]	Gly Lys Pro Thr His Ile Asn Val Ser Val Val Met Ala Glu Ala Asp			
[0617]		325	330	335
[0618]	Gly Thr Cys Tyr			
[0619]		340		
[0620]	<210> 43			
[0621]	<211> 642			
[0622]	<212> PRT			
[0623]	<213> 人工序列(Artificial Sequence)			

[0624] <220>
 [0625] <223> 合成序列-空肠弯曲杆菌亚种空肠血清型0:23/36 (菌株81-176)鞭毛钩相关蛋白2 (Uniprot A0A0H3PIU8)
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 [0630] 20 25 30
 [0631] Ile Asp Pro Tyr Thr Lys Lys Ile Glu Glu Asn Thr Thr Lys Gln Lys
 [0632] 35 40 45
 [0633] Asp Leu Thr Glu Ile Lys Thr Lys Leu Leu Ser Phe Gln Thr Ala Val
 [0634] 50 55 60
 [0635] Ser Ser Leu Ala Asp Ala Thr Val Phe Ala Lys Arg Lys Val Val Gly
 [0636] 65 70 75 80
 [0637] Ser Ile Ser Asp Asn Pro Pro Ala Ser Leu Thr Val Asn Ser Gly Val
 [0638] 85 90 95
 [0639] Ala Leu Gln Ser Met Asn Ile Asn Val Thr Gln Leu Ala Gln Lys Asp
 [0640] 100 105 110
 [0641] Val Tyr Gln Ser Lys Gly Leu Ala Asn Asp Ser Gly Phe Ile Asn Ala
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 [0647] Lys Ile Asn Glu Ala Ser Gly Gly Glu Ile Val Ala Lys Ile Val Asn
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 [0652] 195 200 205
 [0653] Asn Gly Lys Tyr Thr Ser Asp Ser Glu Ala Glu Thr Ile Phe Lys Asn
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 [0655] Leu Gly Trp Glu Leu Asp Thr Thr Ser Ser Ile Asp Pro Ala Lys Asp
 [0656] 225 230 235 240
 [0657] Lys Lys Gly Tyr Gly Ile Lys Asp Ala Ser Leu His Ile Gln Thr Ala
 [0658] 245 250 255
 [0659] Gln Asn Ala Glu Phe Thr Leu Asp Gly Ile Lys Met Phe Arg Ser Ser
 [0660] 260 265 270
 [0661] Asn Thr Val Thr Asp Leu Gly Val Gly Met Thr Leu Thr Leu Asn Lys

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[0663]	Thr Gly Glu Ile Asn Phe Asp Val Gln Gln Asp Phe Glu Gly Val Thr		
[0664]	290	295	300
[0665]	Lys Ala Met Gln Asp Leu Val Asp Ala Tyr Asn Asp Leu Val Thr Asn		
[0666]	305	310	315
[0667]	Leu Asn Ala Ala Thr Asp Tyr Asn Ser Glu Thr Gly Thr Lys Gly Thr		
[0668]	325	330	335
[0669]	Leu Gln Gly Ile Ser Glu Val Asn Ser Ile Arg Ser Ser Ile Leu Ala		
[0670]	340	345	350
[0671]	Asp Leu Phe Asp Ser Gln Val Val Asp Gly Thr Thr Glu Asp Ala Asn		
[0672]	355	360	365
[0673]	Gly Asn Lys Val Asn Thr Lys Val Met Leu Ser Met Gln Asp Phe Gly		
[0674]	370	375	380
[0675]	Leu Ser Leu Asn Asp Ala Gly Thr Leu Ser Phe Asp Ser Ser Lys Phe		
[0676]	385	390	395
[0677]	Glu Gln Lys Val Lys Glu Asp Pro Asp Ser Thr Glu Ser Phe Phe Ser		
[0678]	405	410	415
[0679]	Asn Ile Thr Lys Tyr Glu Asp Ile Asn His Thr Gly Glu Val Ile Lys		
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[0681]	Gln Gly Ser Leu Asn Gln Tyr Leu Asp Ser Ser Gly Thr Gly Asn Lys		
[0682]	435	440	445
[0683]	Gly Leu Asp Phe Lys Pro Gly Asp Phe Thr Ile Val Phe Asn Asn Gln		
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[0685]	Thr Tyr Asp Leu Ser Lys Asn Ser Asp Gly Thr Asn Phe Lys Leu Thr		
[0686]	465	470	475
[0687]	Gly Lys Thr Glu Glu Glu Leu Leu Gln Asn Leu Ala Asn His Ile Asn		
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[0691]	Asn Gly Val Lys Gly Phe Lys Leu Asn Phe Ser Gly Asp Gly Ser Ser		
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[0693]	Asp Phe Ser Ile Lys Gly Asn Ala Thr Ile Leu Lys Glu Leu Gly Leu		
[0694]	530	535	540
[0695]	Ser Asp Val Asn Ile Thr Ser Lys Pro Ile Glu Gly Lys Gly Ile Phe		
[0696]	545	550	555
[0697]	Ser Lys Leu Lys Ala Thr Leu Gln Glu Met Thr Gly Lys Asp Gly Ser		
[0698]	565	570	575
[0699]	Ile Thr Lys Tyr Asp Glu Ser Leu Thr Asn Asn Ile Lys Ser Leu Asn		
[0700]	580	585	590

[0701]	Thr Ser Lys Asp Ser Thr Gln Ala Met Ile Asp Thr Arg Tyr Asp Thr
[0702]	595 600 605
[0703]	Met Ala Asn Gln Trp Leu Gln Tyr Glu Ser Ile Leu Asn Lys Leu Asn
[0704]	610 615 620
[0705]	Gln Gln Leu Asn Thr Val Thr Asn Met Ile Asn Ala Ala Asn Asn Ser
[0706]	625 630 635 640
[0707]	Asn Asn
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[0718]	20 25 30
[0719]	Ile Asp Pro Tyr Thr Lys Lys Ile Glu Glu Asn Thr Thr Lys Gln Lys
[0720]	35 40 45
[0721]	Asp Leu Thr Glu Ile Lys Thr Lys Leu Leu Ser Phe Gln Thr Ala Val
[0722]	50 55 60
[0723]	Ser Ser Leu Ala Asp Ala Thr Val Phe Ala Lys Arg Lys Val Val Gly
[0724]	65 70 75 80
[0725]	Ser Ile Ser Asp Asn Pro Pro Ala Ser Leu Thr Val Asn Ser Gly Val
[0726]	85 90 95
[0727]	Ala Leu Gln Ser Met Asn Ile Asn Val Thr Gln Leu Ala Gln Lys Asp
[0728]	100 105 110
[0729]	Val Tyr Gln Ser Lys Gly Leu Ala Asn Asp Gly Gly Phe Val Asn Ala
[0730]	115 120 125
[0731]	Gln Leu Asn Gly Thr Ala Asp Leu Thr Phe Phe Ser Asn Gly Lys Glu
[0732]	130 135 140
[0733]	Tyr Thr Val Thr Val Asp Lys Asn Thr Thr Tyr Arg Asp Leu Ala Asp
[0734]	145 150 155 160
[0735]	Lys Ile Asn Glu Ala Ser Gly Gly Glu Ile Val Ala Lys Ile Val Asn
[0736]	165 170 175
[0737]	Thr Gly Glu Lys Gly Thr Pro Tyr Arg Leu Thr Leu Thr Ser Lys Glu
[0738]	180 185 190

[0739]	Thr Gly Glu Asp Ser Ala Ile Ser Phe Tyr Ala Gly Lys Lys Asp Ser
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[0741]	Asn Gly Lys Tyr Gln Lys Asp Ile Asn Ala Glu Lys Ile Phe Asp Asp
[0742]	210 215 220
[0743]	Leu Gly Trp Gly Leu Asp Val Ser Ala Ser Ile Asp Pro Asp Lys Asp
[0744]	225 230 235 240
[0745]	Lys Lys Gly Tyr Gly Ile Lys Asp Ala Ser Leu His Ile Gln Thr Ala
[0746]	245 250 255
[0747]	Gln Asn Ala Glu Phe Thr Leu Asp Gly Ile Lys Met Phe Arg Ser Ser
[0748]	260 265 270
[0749]	Asn Thr Val Thr Asp Leu Gly Val Gly Met Thr Leu Thr Leu Asn Lys
[0750]	275 280 285
[0751]	Thr Gly Glu Ile Asn Phe Asp Val Gln Gln Asp Phe Glu Gly Val Thr
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[0755]	Leu Asn Ala Ala Thr Asp Tyr Asn Ser Glu Thr Gly Thr Lys Gly Thr
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[0757]	Leu Gln Gly Ile Ser Glu Val Asn Ser Ile Arg Ser Ser Ile Leu Ala
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[0763]	Leu Ser Leu Asn Asp Ala Gly Thr Leu Ser Phe Asp Ser Ser Lys Phe
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[0773]	Thr Tyr Asp Leu Ser Lys Asn Ser Asp Gly Thr Asn Phe Lys Leu Thr
[0774]	465 470 475 480
[0775]	Gly Lys Thr Glu Glu Glu Leu Leu Gln Asn Leu Ala Asn His Ile Asn
[0776]	485 490 495
[0777]	Ser Lys Gly Ile Glu Gly Leu Lys Val Lys Val Glu Ser Tyr Asn Gln

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[0782]	530	535	540
[0783]	Ser Asp Val Asn Ile Thr Ser Lys Pro Ile Glu Gly Lys Gly Ile Phe		
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[0785]	Ser Lys Leu Lys Ala Thr Leu Gln Glu Met Thr Gly Lys Asp Gly Ser		
[0786]	565	570	575
[0787]	Ile Thr Lys Tyr Asp Glu Ser Leu Thr Asn Asp Ile Lys Ser Leu Asn		
[0788]	580	585	590
[0789]	Thr Ser Lys Asp Ser Thr Gln Ala Met Ile Asp Thr Arg Tyr Asp Thr		
[0790]	595	600	605
[0791]	Met Ala Asn Gln Trp Leu Gln Tyr Glu Ser Ile Leu Asn Lys Leu Asn		
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[0793]	Gln Gln Leu Asn Thr Val Thr Asn Met Ile Asn Ala Ala Asn Asn Ser		
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[0811]	Asp Leu Thr Glu Ile Lys Thr Lys Leu Leu Ser Phe Gln Thr Ala Val		
[0812]	50	55	60
[0813]	Ser Ser Leu Ala Asp Ala Thr Val Phe Ala Lys Arg Lys Val Val Gly		
[0814]	65	70	75
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[0817]	Ala Leu Gln Ser Met Asn Ile Asn Val Thr Gln Leu Ala Gln Lys Asp
[0818]	100 105 110
[0819]	Val Tyr Gln Ser Lys Gly Leu Ala Asn Asp Gly Gly Phe Val Asn Ala
[0820]	115 120 125
[0821]	Gln Leu Asn Gly Thr Ala Asp Leu Thr Phe Phe Ser Asn Gly Lys Glu
[0822]	130 135 140
[0823]	Tyr Thr Val Thr Val Asp Lys Asn Thr Thr Tyr Arg Asp Leu Ala Asp
[0824]	145 150 155 160
[0825]	Lys Ile Asn Glu Ala Ser Gly Gly Glu Ile Val Ala Lys Ile Val Asn
[0826]	165 170 175
[0827]	Thr Gly Glu Lys Gly Thr Pro Tyr Arg Leu Thr Leu Thr Ser Lys Glu
[0828]	180 185 190
[0829]	Thr Gly Glu Asp Ser Ala Ile Ser Phe Tyr Ala Gly Lys Lys Asp Ser
[0830]	195 200 205
[0831]	Asn Gly Lys Tyr Gln Lys Asp Ile Asn Ala Glu Lys Ile Phe Asp Asp
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[0835]	Lys Lys Gly Tyr Gly Ile Lys Asp Ala Ser Leu His Ile Gln Thr Ala
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[0838]	260 265 270
[0839]	Asn Thr Val Thr Asp Leu Gly Val Gly Met Thr Leu Thr Leu Asn Lys
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[0845]	Leu Asn Ala Ala Thr Asp Tyr Asn Ser Glu Thr Gly Thr Lys Gly Thr
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[0847]	Leu Gln Gly Ile Ser Glu Val Asn Ser Ile Arg Ser Ser Ile Leu Ala
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[0862]		450		455		460
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[0865]	Gly Lys Thr Glu Glu Glu Leu Leu Gln Asn Leu Ala Asn His Ile Asn					
[0866]		485		490		495
[0867]	Ser Lys Gly Ile Glu Gly Leu Lys Val Lys Val Glu Ser Tyr Asn Gln					
[0868]		500		505		510
[0869]	Asn Asn Val Thr Gly Phe Arg Leu Asn Phe Ser Gly Asp Gly Ser Ser					
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[0871]	Asp Phe Ser Ile Lys Gly Asp Ala Asn Ile Leu Lys Glu Leu Gly Leu					
[0872]		530		535		540
[0873]	Ser Asp Val Asn Ile Thr Ser Lys Pro Ile Glu Gly Lys Gly Ile Phe					
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[0875]	Ser Lys Leu Lys Ala Thr Leu Gln Glu Met Thr Gly Lys Asp Gly Ser					
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[0877]	Ile Thr Lys Tyr Asp Glu Ser Leu Thr Asn Asp Ile Lys Ser Leu Asn					
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[0881]	Met Ala Asn Gln Trp Leu Gln Tyr Glu Ser Ile Leu Asn Lys Leu Asn					
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[0883]	Gln Gln Leu Asn Thr Val Thr Asn Met Ile Asn Ala Ala Asn Asn Ser					
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[0887]	<211> 642					
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[0900]	Asp Leu Thr Glu Ile Lys Thr Lys Leu Leu Ser Phe Gln Thr Ala Val			
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[0902]	Ser Ser Leu Ala Asp Ala Thr Val Phe Ala Lys Arg Lys Val Val Gly			
[0903]	65	70	75	80
[0904]	Ser Ile Ser Asp Asn Pro Pro Ala Ser Leu Thr Val Asn Ser Gly Val			
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[0906]	Ala Leu Gln Ser Met Asn Ile Asn Val Thr Gln Leu Ala Gln Lys Asp			
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[0908]	Val Tyr Gln Ser Gln Gly Leu Ala Asn Asp Ser Gly Phe Ile Asn Ala			
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[0912]	Tyr Thr Val Thr Val Asp Lys Asn Thr Thr Tyr Arg Asp Leu Ala Asp			
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[0914]	Lys Ile Asn Glu Ala Ser Gly Gly Glu Ile Val Ala Lys Ile Val Asn			
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[0916]	Thr Gly Glu Lys Gly Thr Pro Tyr Arg Leu Thr Leu Thr Ser Lys Glu			
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[0918]	Thr Gly Glu Asp Ser Ala Ile Ser Phe Tyr Ala Gly Lys Lys Asp Ala			
[0919]	195	200	205	
[0920]	Gln Gly Gln Tyr Lys Ser Asp Leu Glu Ala Glu Lys Ile Phe Lys Ser			
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[0922]	Leu Gly Trp Glu Leu Asp Thr Thr Ser Ser Ile Asp Pro Ala Lys Asp			
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[0924]	Lys Lys Gly Tyr Gly Ile Lys Asp Ala Ser Leu His Ile Gln Thr Ala			
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[0926]	Gln Asn Ala Glu Phe Thr Leu Asp Gly Ile Lys Met Phe Arg Ser Ser			
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[0928]	Asn Thr Val Thr Asp Leu Gly Val Gly Met Thr Leu Thr Leu Asn Lys			
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[0936]	Leu Gln Gly Ile Ser Glu Val Asn Ser Ile Arg Ser Ser Ile Leu Ala
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[0967]	580 585 590
[0968]	Thr Ser Lys Asp Ser Thr Gln Ala Met Ile Asp Thr Arg Tyr Asp Thr
[0969]	595 600 605
[0970]	Met Ala Asn Gln Trp Leu Gln Tyr Glu Ser Ile Leu Asn Lys Leu Asn
[0971]	610 615 620
[0972]	Gln Gln Leu Asn Thr Val Thr Asn Met Ile Asn Ala Ala Asn Asn Ser

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[0986]	Ile Asp Pro Tyr Thr Lys Lys Ile Glu Glu Asn Thr Thr Lys Gln Lys			
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[0988]	Asp Leu Thr Glu Ile Lys Thr Lys Leu Leu Ser Phe Gln Thr Ala Val			
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[0990]	Ser Ser Leu Ala Asp Ala Thr Val Phe Ala Lys Arg Lys Val Val Gly			
[0991]		65	70	75
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[0996]	Val Tyr Gln Ser Lys Gly Leu Ala Asn Asp Ser Gly Phe Ile Asn Ala			
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[1002]	Lys Ile Asn Glu Ala Ser Gly Gly Glu Ile Val Ala Lys Ile Val Asn			
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[1004]	Thr Gly Glu Lys Gly Thr Pro Tyr Arg Leu Thr Leu Thr Ser Lys Glu			
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[1008]	Asn Gly Lys Tyr Thr Ser Asp Ser Glu Ala Glu Thr Ile Phe Lys Asn			
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[1010]	Leu Gly Trp Glu Leu Asp Thr Thr Ser Ser Ile Asp Pro Ala Lys Asp			

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 [1061] 625 630 635 640
 [1062] Asn Asn
 [1063] <210> 48
 [1064] <211> 642
 [1065] <212> PRT
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 [1086] Gln Leu Asn Gly Thr Ala Asp Leu Thr Phe Phe Ser Asn Gly Lys Glu
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[1088]	Tyr Thr Val Thr Val Asp Lys Asn Thr Thr Tyr Arg Asp Leu Ala Asp
[1089]	145 150 155 160
[1090]	Lys Ile Asn Glu Ala Ser Gly Gly Glu Ile Val Ala Lys Ile Val Asn
[1091]	165 170 175
[1092]	Thr Gly Glu Lys Gly Thr Pro Tyr Arg Leu Thr Leu Thr Ser Lys Glu
[1093]	180 185 190
[1094]	Thr Gly Glu Asp Ser Ala Ile Ser Phe Tyr Ala Gly Lys Lys Asp Ser
[1095]	195 200 205
[1096]	Asn Gly Lys Tyr Gln Lys Asp Thr Asn Ala Glu Lys Ile Phe Asp Asp
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[1098]	Leu Gly Trp Gly Leu Asp Ala Ser Ala Ser Ile Asp Pro Ala Lys Asp
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[1102]	Gln Asn Ala Glu Phe Thr Leu Asp Gly Ile Lys Met Phe Arg Ser Ser
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[1104]	Asn Thr Val Thr Asp Leu Gly Val Gly Met Thr Leu Thr Leu Asn Lys
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[1106]	Thr Gly Glu Ile Asn Phe Asp Val Gln Gln Asp Phe Glu Gly Val Thr
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[1108]	Lys Ala Met Gln Asp Leu Val Asp Ala Tyr Asn Asp Leu Val Thr Asn
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[1110]	Leu Asn Ala Ala Thr Asp Tyr Asn Ser Glu Thr Gly Thr Lys Gly Thr
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[1112]	Leu Gln Gly Ile Ser Glu Val Asn Ser Ile Arg Ser Ser Ile Leu Ala
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[1143]		580	585 590
[1144]	Thr Ser Lys Asp Ser Thr Gln Ala Met Ile Asp Thr Arg Tyr Asp Thr		
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[1165]	Asp Leu Thr Glu Ile Lys Thr Lys Leu Leu Ser Phe Gln Thr Ala Val		

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[1171]	Ala Leu Gln Ser Met Asn Ile Asn Val Thr Gln Leu Ala Gln Lys Asp		
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[1193]	Asn Thr Val Thr Asp Leu Gly Val Gly Met Thr Leu Thr Leu Asn Lys		
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[1207]	Leu Ser Leu Asn Asp Ala Gly Thr Leu Ser Phe Asp Ser Ser Lys Phe
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[1213]	Thr Gly Ser Leu Ser Lys Tyr Leu Asn Ser Asn Gly Gly Asn Thr Asn
[1214]	435 440 445
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[1216]	450 455 460
[1217]	Thr Tyr Asp Leu Ser Lys Asn Ser Asp Gly Ile Asn Phe Lys Leu Thr
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[1219]	Gly Lys Thr Glu Glu Glu Leu Leu Gln Asn Leu Ala Asn His Ile Asn
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[1221]	Ser Lys Gly Ile Glu Gly Leu Lys Val Lys Val Glu Ser Tyr Asn Gln
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[1223]	Asn Asn Val Thr Gly Phe Arg Leu Asn Phe Ser Gly Asp Gly Ser Ser
[1224]	515 520 525
[1225]	Asp Phe Ser Ile Lys Gly Asp Ala Asn Ile Leu Lys Glu Leu Gly Leu
[1226]	530 535 540
[1227]	Ser Asp Val Asn Ile Thr Ser Lys Pro Ile Glu Gly Lys Gly Ile Phe
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[1229]	Ser Lys Leu Lys Ala Thr Leu Gln Glu Met Thr Gly Lys Asp Gly Ser
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[1231]	Ile Thr Lys Tyr Asp Glu Ser Leu Thr Asn Asp Ile Lys Ser Leu Asn
[1232]	580 585 590
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[1235]	Met Ala Asn Gln Trp Leu Gln Tyr Glu Ser Ile Leu Asn Lys Leu Asn
[1236]	610 615 620
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[1245] <223> 合成序列-鞭毛丝加帽蛋白Flid [空肠弯曲杆菌] NCBI参照序列: WP_004306838.1

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[1251] Ile Asp Pro Tyr Thr Lys Lys Ile Glu Glu Asn Thr Thr Lys Gln Lys

[1252] 35 40 45

[1253] Asp Leu Thr Glu Ile Lys Thr Lys Leu Leu Ser Phe Gln Thr Ala Val

[1254] 50 55 60

[1255] Ser Ser Leu Ala Asp Ala Thr Val Phe Ala Lys Arg Lys Val Val Gly

[1256] 65 70 75 80

[1257] Ser Ile Ser Asp Asn Pro Pro Ala Ser Leu Thr Val Asn Ser Gly Val

[1258] 85 90 95

[1259] Ala Leu Gln Ser Met Asn Ile Asn Val Thr Gln Leu Ala Gln Lys Asp

[1260] 100 105 110

[1261] Val Tyr Gln Ser Gln Gly Leu Ala Asn Asp Gly Gly Phe Val Asn Ala

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[1263] Gln Leu Asn Gly Thr Ala Asp Leu Thr Phe Phe Ser Asn Gly Lys Glu

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[1265] Tyr Thr Val Thr Val Asp Lys Asn Thr Thr Tyr Arg Asp Leu Ala Asp

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[1271] Thr Gly Glu Asp Ser Ala Ile Ser Phe Tyr Ala Gly Lys Lys Asp Ala

[1272] 195 200 205

[1273] Gln Gly Gln Tyr Lys Ser Asp Leu Glu Ala Glu Lys Ile Phe Lys Ser

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[1275] Leu Gly Trp Glu Leu Asp Thr Thr Ser Ser Ile Asp Pro Ala Lys Asp

[1276] 225 230 235 240

[1277] Lys Lys Gly Tyr Gly Ile Lys Asp Ala Ser Leu His Ile Gln Thr Ala

[1278] 245 250 255

[1279] Gln Asn Ala Glu Phe Thr Leu Asp Gly Ile Lys Met Phe Arg Ser Ser

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[1315]	Ser Asp Val Asn Ile Ser Ser Lys Pro Ile Glu Gly Lys Gly Ile Phe		
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[1317]	Ser Lys Leu Lys Ala Thr Leu Gln Glu Met Thr Gly Lys Asp Gly Ser		
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[1319]	Ile Thr Lys Tyr Asp Glu Ser Leu Thr Asn Asp Ile Lys Ser Leu Asn		
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[1321]	Thr Ser Lys Asp Ser Thr Gln Val Met Ile Asp Thr Arg Tyr Asp Thr
[1322]	595 600 605
[1323]	Met Ala Asn Gln Trp Leu Gln Tyr Glu Ser Ile Leu Asn Lys Leu Asn
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[1339]	Ile Asp Pro Tyr Thr Lys Lys Ile Glu Glu Asn Thr Thr Lys Gln Lys
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[1341]	Asp Leu Thr Glu Ile Lys Thr Lys Leu Leu Ser Phe Gln Thr Ala Val
[1342]	50 55 60
[1343]	Ser Ser Leu Ala Asp Ala Thr Val Phe Ala Lys Arg Lys Val Val Gly
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[1345]	Ser Ile Ser Asp Asn Pro Pro Ala Ser Leu Thr Val Asn Ser Gly Val
[1346]	85 90 95
[1347]	Ala Leu Gln Ser Met Asn Ile Asn Val Thr Gln Leu Ala Gln Lys Asp
[1348]	100 105 110
[1349]	Val Tyr Gln Ser Lys Gly Leu Ala Asn Asp Ser Gly Phe Val Asn Ala
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[1351]	Gln Leu Asn Gly Thr Ala Asp Leu Thr Phe Phe Ser Asn Gly Lys Glu
[1352]	130 135 140
[1353]	Tyr Thr Val Thr Val Asp Lys Asn Thr Thr Tyr Arg Asp Leu Ala Asp
[1354]	145 150 155 160
[1355]	Lys Ile Asn Glu Ala Ser Gly Gly Glu Ile Val Ala Lys Ile Val Asn
[1356]	165 170 175
[1357]	Thr Gly Glu Lys Gly Thr Pro Tyr Arg Leu Thr Leu Thr Ser Lys Glu
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[1359]	Thr Gly Glu Asp Ser Ala Ile Ser Phe Tyr Ala Gly Lys Lys Asp Ser
[1360]	195 200 205
[1361]	Asn Gly Lys Tyr Gln Lys Asp Thr Asn Ala Glu Lys Ile Phe Asp Asp
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[1364]	225 230 235 240
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[1403]	Ser Asp Val Asn Ile Thr Ser Lys Pro Ile Glu Gly Lys Gly Ile Phe		
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[1405]	Ser Lys Leu Lys Ala Thr Leu Gln Glu Met Thr Gly Lys Asp Gly Ser		
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[1407]	Ile Thr Lys Tyr Asp Glu Ser Leu Thr Asn Asp Ile Lys Ser Leu Asn		
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[1409]	Thr Ser Lys Asp Ser Thr Gln Ala Met Ile Asp Thr Arg Tyr Asp Thr		
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[1431]	Ser Ser Leu Ala Asp Ala Thr Val Phe Ala Lys Arg Lys Val Val Gly		
[1432]	65	70	75
[1433]	Ser Ile Ser Asp Asn Pro Pro Ala Ser Leu Thr Val Asn Ser Gly Val		
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[1435]	Ala Leu Gln Ser Met Asn Ile Asn Val Thr Gln Leu Ala Gln Lys Asp		

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[1474]																		415

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[1480]	450 455 460
[1481]	Thr Tyr Asp Leu Ser Lys Asn Ser Asp Gly Thr Asn Phe Lys Leu Thr
[1482]	465 470 475 480
[1483]	Gly Lys Thr Glu Glu Glu Leu Leu Gln Asn Leu Ala Asn His Ile Asn
[1484]	485 490 495
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[1572]	Gly Lys Thr Glu Glu Glu Leu Leu Gln Asn Leu Ala Asn His Ile Asn					
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[1579]		530		535		540
[1580]	Ser Asp Val Asn Ile Thr Ser Lys Pro Ile Glu Gly Lys Gly Ile Phe					
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[1582]	Ser Lys Leu Lys Ala Thr Leu Gln Glu Met Thr Gly Lys Asp Gly Ser					
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[1584]	Ile Thr Lys Tyr Asp Glu Ser Leu Thr Asn Asp Ile Lys Ser Leu Asn					
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[1767]	610 615 620
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[2016]	485	490	495
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						560

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[2290]	565 570 575
[2291]	Ser Ile Thr Lys Tyr Asp Glu Ser Leu Thr Asn Asp Ile Lys Ser Leu
[2292]	580 585 590
[2293]	Asn Thr Ser Lys Asp Ser Thr Gln Ala Met Ile Asp Thr Arg Tyr Asp
[2294]	595 600 605
[2295]	Thr Met Ala Asn Gln Trp Leu Gln Tyr Glu Ser Ile Leu Asn Lys Leu
[2296]	610 615 620
[2297]	Asn Gln Gln Leu Asn Thr Val Thr Asn Met Ile Asn Ala Ala Asn Asn
[2298]	625 630 635 640
[2299]	Ser Asn Asn
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[2308]	1 5 10 15
[2309]	Thr Gln Asp Thr Ile Asp Lys Leu Lys Glu Ala Glu Gln Lys Ala Arg
[2310]	20 25 30
[2311]	Ile Asp Pro Tyr Thr Lys Lys Ile Glu Glu Asn Thr Thr Lys Gln Lys
[2312]	35 40 45
[2313]	Asp Leu Thr Glu Ile Lys Thr Lys Leu Leu Ser Phe Gln Thr Ala Val
[2314]	50 55 60
[2315]	Ser Ser Leu Ala Asp Ala Thr Val Phe Ala Lys Arg Lys Val Val Gly
[2316]	65 70 75 80
[2317]	Ser Ile Ser Asp Asn Pro Pro Ala Ser Leu Thr Val Asn Ser Gly Val
[2318]	85 90 95
[2319]	Ala Leu Gln Ser Met Asn Ile Asn Val Thr Gln Leu Ala Gln Lys Asp
[2320]	100 105 110
[2321]	Val Tyr Gln Ser Gln Gly Leu Ala Asn Asp Ser Gly Phe Ile Asn Ala
[2322]	115 120 125
[2323]	Asn Leu Ala Gly Thr Thr Asp Leu Thr Phe Phe Ser Asn Gly Lys Glu
[2324]	130 135 140
[2325]	Tyr Thr Val Thr Val Asp Lys Asn Thr Thr Tyr Arg Asp Leu Ala Asp
[2326]	145 150 155 160
[2327]	Lys Ile Asn Glu Ala Ser Gly Gly Glu Ile Val Ala Lys Ile Val Asn

[2328]		165		170		175
[2329]	Thr Gly Glu Lys Gly Thr Pro Tyr Arg Leu Thr Leu Thr Ser Lys Glu					
[2330]		180		185		190
[2331]	Thr Gly Glu Asp Ser Ala Ile Ser Phe Tyr Ala Gly Lys Lys Asp Ala					
[2332]		195		200		205
[2333]	Gln Gly Gln Tyr Gln Ser Asp Pro Glu Ala Glu Lys Ile Phe Ser Asn					
[2334]		210		215		220
[2335]	Leu Gly Trp Glu Leu Asp Lys Thr Thr Gln Thr Ile Asp Pro Ala Lys					
[2336]		225		230		235
[2337]	Asp Lys Lys Gly Tyr Gly Ile Lys Asp Ala Ser Leu His Ile Gln Thr					
[2338]		245		250		255
[2339]	Ala Gln Asn Ala Glu Phe Thr Leu Asp Gly Ile Lys Met Phe Arg Ser					
[2340]		260		265		270
[2341]	Ser Asn Thr Val Thr Asp Leu Gly Val Gly Met Thr Leu Thr Leu Asn					
[2342]		275		280		285
[2343]	Lys Thr Gly Glu Ile Asn Phe Asp Val Gln Gln Asp Phe Glu Gly Val					
[2344]		290		295		300
[2345]	Thr Lys Ala Met Gln Asp Leu Val Asp Ala Tyr Asn Asp Leu Val Thr					
[2346]		305		310		315
[2347]	Asn Leu Asn Ala Ala Thr Asp Tyr Asn Ser Glu Thr Gly Thr Lys Gly					
[2348]		325		330		335
[2349]	Thr Leu Gln Gly Ile Ser Glu Val Asn Ser Ile Arg Ser Ser Ile Leu					
[2350]		340		345		350
[2351]	Ala Asp Leu Phe Asp Ser Gln Val Val Asp Gly Thr Thr Glu Asp Ala					
[2352]		355		360		365
[2353]	Asn Gly Asn Lys Val Asn Thr Lys Val Met Leu Ser Met Gln Asp Phe					
[2354]		370		375		380
[2355]	Gly Leu Ser Leu Asn Asp Ala Gly Thr Leu Ser Phe Asp Ser Ser Lys					
[2356]		385		390		395
[2357]	Phe Glu Gln Lys Val Lys Glu Asp Pro Asp Ser Thr Glu Ser Phe Phe					
[2358]		405		410		415
[2359]	Ser Asn Ile Thr Lys Tyr Glu Asp Ile Asn His Thr Gly Glu Val Ile					
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[2361]	Lys Thr Gly Ser Leu Ser Lys Tyr Leu Asn Ser Asn Gly Gly Asn Thr					
[2362]		435		440		445
[2363]	Asn Gly Leu Glu Phe Lys Pro Gly Asp Phe Thr Ile Val Phe Asn Asn					
[2364]		450		455		460
[2365]	Gln Thr Tyr Asp Leu Ser Lys Asn Ser Asp Gly Thr Asn Phe Lys Leu					
[2366]		465		470		475
						480

[2367]	Thr Gly Lys Thr Glu Glu Glu Leu Leu Gln Asn Leu Ala Asn His Ile
[2368]	485 490 495
[2369]	Asn Ser Lys Gly Ile Glu Gly Leu Lys Val Lys Val Glu Ser Tyr Asn
[2370]	500 505 510
[2371]	Gln Asn Asn Val Thr Gly Phe Arg Leu Asn Phe Ser Gly Asp Gly Ser
[2372]	515 520 525
[2373]	Ser Asp Phe Ser Ile Lys Gly Asp Ala Asn Ile Leu Lys Glu Leu Gly
[2374]	530 535 540
[2375]	Leu Ser Asp Val Asn Ile Thr Ser Lys Pro Ile Glu Gly Lys Gly Ile
[2376]	545 550 555 560
[2377]	Phe Ser Lys Leu Lys Ala Thr Leu Gln Glu Met Thr Gly Lys Asp Gly
[2378]	565 570 575
[2379]	Ser Ile Thr Lys Tyr Asp Glu Ser Leu Thr Asn Asp Ile Lys Ser Leu
[2380]	580 585 590
[2381]	Asn Thr Ser Lys Asp Ser Thr Gln Ala Met Ile Asp Thr Arg Tyr Asp
[2382]	595 600 605
[2383]	Thr Met Ala Asn Gln Trp Leu Gln Tyr Glu Ser Ile Leu Asn Lys Leu
[2384]	610 615 620
[2385]	Asn Gln Gln Leu Asn Thr Val Thr Asn Met Ile Asn Ala Ala Asn Asn
[2386]	625 630 635 640
[2387]	Ser Asn Asn
[2388]	<210> 63
[2389]	<211> 643
[2390]	<212> PRT
[2391]	<213> 人工序列(Artificial Sequence)
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[2398]	Thr Gln Asp Thr Ile Asp Lys Leu Lys Glu Ala Glu Gln Lys Ala Arg
[2399]	20 25 30
[2400]	Ile Asp Pro Tyr Thr Lys Lys Ile Glu Glu Asn Thr Thr Lys Gln Lys
[2401]	35 40 45
[2402]	Asp Leu Thr Glu Ile Lys Thr Lys Leu Leu Ser Phe Gln Thr Ala Val
[2403]	50 55 60
[2404]	Ser Ser Leu Ala Asp Ala Thr Val Phe Ala Lys Arg Lys Val Val Gly
[2405]	65 70 75 80

[2406]	Ser Ile Ser Asp Asn Pro Pro Ala Ser Leu Thr Val Asn Ser Gly Val
[2407]	85 90 95
[2408]	Ala Leu Gln Ser Met Asn Ile Asn Val Thr Gln Leu Ala Gln Lys Asp
[2409]	100 105 110
[2410]	Val Tyr Gln Ser Lys Gly Leu Ala Asn Asp Ser Gly Phe Ile Asn Ala
[2411]	115 120 125
[2412]	Asn Leu Thr Gly Thr Thr Asp Leu Thr Phe Phe Ser Asn Gly Lys Glu
[2413]	130 135 140
[2414]	Tyr Thr Val Thr Val Asp Lys Ser Thr Thr Tyr Arg Asp Leu Ala Asp
[2415]	145 150 155 160
[2416]	Lys Ile Asn Glu Ala Ser Gly Gly Glu Ile Val Ala Lys Ile Val Asn
[2417]	165 170 175
[2418]	Thr Gly Glu Lys Gly Thr Pro Tyr Arg Leu Thr Leu Thr Ser Lys Glu
[2419]	180 185 190
[2420]	Thr Gly Glu Asp Ser Ala Ile Ser Phe Tyr Ala Gly Lys Lys Asp Ala
[2421]	195 200 205
[2422]	Gln Gly Gln Tyr Lys Ser Asp Ser Glu Ala Glu Lys Ile Phe Ser Asn
[2423]	210 215 220
[2424]	Leu Gly Trp Glu Leu Asp Lys Thr Thr Gln Thr Ile Asp Pro Ala Lys
[2425]	225 230 235 240
[2426]	Asp Lys Lys Gly Tyr Gly Ile Lys Asp Ala Ser Leu His Ile Gln Thr
[2427]	245 250 255
[2428]	Ala Gln Asn Ala Glu Phe Thr Leu Asp Gly Ile Lys Met Phe Arg Ser
[2429]	260 265 270
[2430]	Ser Asn Thr Val Thr Asp Leu Gly Val Gly Met Thr Leu Thr Leu Asn
[2431]	275 280 285
[2432]	Lys Thr Gly Glu Ile Asn Phe Asp Val Gln Gln Asp Phe Glu Gly Val
[2433]	290 295 300
[2434]	Thr Lys Ala Met Gln Asp Leu Val Asp Ala Tyr Asn Asp Leu Val Thr
[2435]	305 310 315 320
[2436]	Asn Leu Asn Ala Ala Thr Asp Tyr Asn Ser Glu Thr Gly Thr Lys Gly
[2437]	325 330 335
[2438]	Thr Leu Gln Gly Ile Ser Glu Val Asn Ser Ile Arg Ser Ser Ile Leu
[2439]	340 345 350
[2440]	Ala Asp Leu Phe Asp Ser Gln Val Val Asp Gly Thr Thr Glu Asp Ala
[2441]	355 360 365
[2442]	Asn Gly Asn Lys Val Asn Thr Lys Val Met Leu Ser Met Gln Asp Phe
[2443]	370 375 380
[2444]	Gly Leu Ser Leu Asn Asp Ala Gly Thr Leu Ser Phe Asp Ser Ser Lys

[2445]	385	390	395	400
[2446]	Phe Glu Gln Lys Val Lys Glu Asp Pro Asp Ser Thr Glu Ser Phe Phe			
[2447]	405	410	415	
[2448]	Ser Asn Ile Thr Lys Tyr Glu Asp Ile Asn His Thr Gly Glu Val Ile			
[2449]	420	425	430	
[2450]	Lys Gln Gly Ser Leu Asn Gln Tyr Leu Asp Ser Ser Gly Thr Gly Asn			
[2451]	435	440	445	
[2452]	Lys Gly Leu Glu Phe Lys Pro Gly Gly Phe Thr Ile Val Phe Asn Asn			
[2453]	450	455	460	
[2454]	Gln Thr Tyr Asp Leu Ser Lys Asn Ser Asp Gly Thr Asn Phe Lys Leu			
[2455]	465	470	475	480
[2456]	Thr Gly Lys Thr Glu Glu Glu Leu Leu Gln Asn Leu Ala Asn His Ile			
[2457]	485	490	495	
[2458]	Asn Ser Lys Gly Ile Glu Gly Leu Lys Val Lys Val Glu Ser Tyr Asp			
[2459]	500	505	510	
[2460]	Gln Asn Gly Val Lys Gly Phe Lys Leu Asn Phe Ser Gly Asp Gly Ser			
[2461]	515	520	525	
[2462]	Ser Asp Phe Ser Ile Lys Gly Asp Ala Asn Ile Leu Lys Glu Leu Gly			
[2463]	530	535	540	
[2464]	Leu Ser Asp Val Asn Ile Thr Ser Lys Pro Ile Glu Gly Lys Gly Ile			
[2465]	545	550	555	560
[2466]	Phe Ser Lys Leu Lys Ala Thr Leu Gln Glu Met Thr Gly Lys Asp Gly			
[2467]	565	570	575	
[2468]	Ser Ile Thr Lys Tyr Asp Glu Ser Leu Thr Asn Asp Ile Lys Ser Leu			
[2469]	580	585	590	
[2470]	Asn Thr Ser Lys Asp Ser Thr Gln Ala Met Ile Asp Thr Arg Tyr Asp			
[2471]	595	600	605	
[2472]	Thr Met Ala Asn Gln Trp Leu Gln Tyr Glu Ser Ile Leu Asn Lys Leu			
[2473]	610	615	620	
[2474]	Asn Gln Gln Leu Asn Thr Val Thr Asn Met Ile Asn Ala Ala Asn Asn			
[2475]	625	630	635	640
[2476]	Ser Asn Asn			
[2477]	<210> 64			
[2478]	<211> 642			
[2479]	<212> PRT			
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[2481]	<220>			
[2482]	<223> 合成序列- 鞭毛钩相关			
[2483]	蛋白Flid [空肠弯曲杆菌亚种空肠260.94]			

[2484] GenBank: EAQ58732.1
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 [2489] 20 25 30
 [2490] Ile Asp Pro Tyr Thr Lys Lys Ile Glu Glu Asn Thr Thr Lys Gln Lys
 [2491] 35 40 45
 [2492] Asp Leu Thr Glu Ile Lys Thr Lys Leu Leu Ser Phe Gln Thr Ala Val
 [2493] 50 55 60
 [2494] Ser Ser Leu Ala Asp Ala Thr Val Phe Ala Lys Arg Lys Val Val Gly
 [2495] 65 70 75 80
 [2496] Ser Ile Ser Asp Asn Pro Pro Ala Ser Leu Thr Val Asn Ser Gly Val
 [2497] 85 90 95
 [2498] Ala Leu Gln Ser Met Asn Ile Asn Val Thr Gln Leu Ala Gln Lys Asp
 [2499] 100 105 110
 [2500] Val Tyr Gln Ser Lys Gly Leu Ala Asn Asp Gly Gly Phe Val Asn Ala
 [2501] 115 120 125
 [2502] Gln Leu Asn Gly Thr Ala Asp Leu Thr Phe Phe Ser Asn Gly Lys Glu
 [2503] 130 135 140
 [2504] Tyr Thr Val Thr Val Asp Lys Asn Thr Thr Tyr Arg Asp Leu Ala Asp
 [2505] 145 150 155 160
 [2506] Lys Ile Asn Glu Ala Ser Gly Gly Glu Ile Val Ala Lys Ile Val Asn
 [2507] 165 170 175
 [2508] Thr Gly Glu Lys Gly Thr Pro Tyr Arg Leu Thr Leu Thr Ser Lys Glu
 [2509] 180 185 190
 [2510] Thr Gly Glu Asp Ser Ala Ile Ser Phe Tyr Ala Gly Lys Lys Asp Ser
 [2511] 195 200 205
 [2512] Asn Gly Lys Tyr Gln Lys Asp Thr Asn Ala Glu Lys Ile Phe Asp Asp
 [2513] 210 215 220
 [2514] Leu Gly Trp Gly Leu Asp Ala Ser Ala Ser Ile Asp Pro Ala Lys Asp
 [2515] 225 230 235 240
 [2516] Lys Lys Gly Tyr Gly Ile Lys Asp Ala Ser Leu His Ile Gln Thr Ala
 [2517] 245 250 255
 [2518] Gln Asn Ala Glu Phe Thr Leu Asp Gly Ile Lys Met Phe Arg Ser Ser
 [2519] 260 265 270
 [2520] Asn Thr Val Thr Asp Leu Gly Val Gly Met Thr Leu Thr Leu Asn Lys
 [2521] 275 280 285
 [2522] Thr Gly Glu Ile Asn Phe Asp Val Gln Gln Asp Phe Glu Gly Val Thr

[2523]	290	295	300
[2524]	Lys Ala Met Gln Asp Leu Val Asp Ala Tyr Asn Asp Leu Val Thr Asn		
[2525]	305	310	315
[2526]	Leu Asn Ala Ala Thr Asp Tyr Asn Ser Glu Thr Gly Thr Lys Gly Thr		
[2527]		325	330
[2528]	Leu Gln Gly Ile Ser Glu Val Asn Ser Ile Arg Ser Ser Ile Leu Ala		
[2529]		340	345
[2530]	Asp Leu Phe Asp Ser Gln Val Val Asp Gly Thr Thr Glu Asp Ala Asn		
[2531]		355	360
[2532]	Gly Asn Lys Val Asn Thr Lys Val Met Leu Ser Met Gln Asp Phe Gly		
[2533]		370	375
[2534]	Leu Ser Leu Asn Asp Ala Gly Thr Leu Asn Phe Asp Ser Ser Lys Phe		
[2535]		385	390
[2536]	Glu Gln Lys Val Lys Glu Asp Pro Asp Ser Ala Glu Ser Phe Phe Ser		
[2537]		405	410
[2538]	Asn Ile Thr Lys Tyr Glu Asp Ile Asn His Thr Gly Glu Ile Ile Lys		
[2539]		420	425
[2540]	Thr Gly Asn Leu Ser Lys Tyr Leu Asn Ser Asn Gly Gly Asn Thr Asn		
[2541]		435	440
[2542]	Gly Leu Asp Phe Lys Pro Gly Asp Phe Thr Ile Val Phe Asn Asn Gln		
[2543]		450	455
[2544]	Thr Tyr Asp Leu Ser Lys Asn Ser Asp Gly Thr Asn Phe Lys Leu Thr		
[2545]		465	470
[2546]	Gly Lys Thr Glu Glu Glu Leu Leu Gln Asn Leu Ala Asn His Ile Asn		
[2547]		485	490
[2548]	Ser Lys Gly Ile Glu Gly Leu Lys Val Lys Val Glu Ser Tyr Asp Gln		
[2549]		500	505
[2550]	Asn Asn Val Lys Gly Phe Lys Leu Asn Phe Ser Gly Asp Gly Ser Ser		
[2551]		515	520
[2552]	Asp Phe Ser Ile Lys Gly Asp Ala Ser Ile Leu Lys Glu Leu Gly Leu		
[2553]		530	535
[2554]	Ser Asp Val Asn Ile Ile Ser Lys Pro Ile Glu Gly Lys Gly Ile Phe		
[2555]		545	550
[2556]	Ser Lys Leu Lys Ala Thr Leu Gln Glu Met Thr Gly Lys Asp Gly Ser		
[2557]		565	570
[2558]	Ile Thr Lys Tyr Asp Glu Ser Leu Thr Asn Asp Ile Lys Ser Leu Asn		
[2559]		580	585
[2560]	Thr Ser Lys Asp Ser Thr Gln Ala Met Ile Asp Thr Arg Tyr Asp Thr		
[2561]		595	600
			605

[2562] Met Ala Asn Gln Trp Leu Gln Tyr Glu Ser Ile Leu Asn Lys Leu Asn
 [2563] 610 615 620
 [2564] Gln Gln Leu Asn Thr Val Thr Asn Met Ile Asn Ala Ala Asn Asn Ser
 [2565] 625 630 635 640
 [2566] Asn Asn
 [2567] <210> 65
 [2568] <211> 642
 [2569] <212> PRT
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 [2571] <220>
 [2572] <223> 合成序列- 鞭毛钩相关
 [2573] 蛋白Flid [空肠弯曲杆菌亚种空肠CF93-6]
 [2574] GenBank: EAQ57731.1
 [2575] <400> 65
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 [2578] Thr Gln Asp Thr Ile Asp Lys Leu Lys Glu Ala Glu Gln Lys Ala Arg
 [2579] 20 25 30
 [2580] Ile Asp Pro Tyr Thr Lys Lys Ile Glu Glu Asn Thr Thr Lys Gln Lys
 [2581] 35 40 45
 [2582] Asp Leu Thr Glu Ile Lys Thr Lys Leu Leu Ser Phe Gln Thr Ala Val
 [2583] 50 55 60
 [2584] Ser Ser Leu Ala Asp Ala Thr Val Phe Ala Lys Arg Lys Val Val Gly
 [2585] 65 70 75 80
 [2586] Ser Ile Ser Asp Asn Pro Pro Ala Ser Leu Thr Val Asn Ser Gly Val
 [2587] 85 90 95
 [2588] Ala Leu Gln Ser Met Asn Ile Asn Val Thr Gln Leu Ala Gln Lys Asp
 [2589] 100 105 110
 [2590] Val Tyr Gln Ser Lys Gly Leu Ala Asn Asp Gly Gly Phe Val Asn Ala
 [2591] 115 120 125
 [2592] Gln Leu Asn Gly Thr Ala Asp Leu Thr Phe Phe Ser Asn Gly Lys Glu
 [2593] 130 135 140
 [2594] Tyr Thr Val Thr Val Asp Lys Asn Thr Thr Tyr Arg Asp Leu Ala Asp
 [2595] 145 150 155 160
 [2596] Lys Ile Asn Glu Ala Ser Gly Gly Glu Ile Val Ala Lys Ile Val Asn
 [2597] 165 170 175
 [2598] Thr Gly Glu Lys Gly Thr Pro Tyr Arg Leu Thr Leu Thr Ser Lys Glu
 [2599] 180 185 190
 [2600] Thr Gly Glu Asp Ser Ala Ile Ser Phe Tyr Ala Gly Lys Lys Asp Ser

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[2602]	Asn Gly Lys Tyr Gln Lys Asp Ile Asn Ala Glu Lys Ile Phe Asp Asp		
[2603]	210	215	220
[2604]	Leu Gly Trp Gly Leu Asp Val Ser Ala Ser Ile Asp Pro Asp Lys Asp		
[2605]	225	230	235
[2606]	Lys Lys Gly Tyr Gly Ile Lys Asp Ala Ser Leu His Ile Gln Thr Ala		
[2607]	245	250	255
[2608]	Gln Asn Ala Glu Phe Thr Leu Asp Gly Ile Lys Met Phe Arg Ser Ser		
[2609]	260	265	270
[2610]	Asn Thr Val Thr Asp Leu Gly Val Gly Met Thr Leu Thr Leu Asn Lys		
[2611]	275	280	285
[2612]	Thr Gly Glu Ile Asn Phe Asp Val Gln Gln Asp Phe Glu Gly Val Thr		
[2613]	290	295	300
[2614]	Lys Ala Met Gln Asp Leu Val Asp Ala Tyr Asn Asp Leu Val Thr Asn		
[2615]	305	310	315
[2616]	Leu Asn Ala Ala Thr Asp Tyr Asn Ser Glu Thr Gly Thr Lys Gly Thr		
[2617]	325	330	335
[2618]	Leu Gln Gly Ile Ser Glu Val Asn Ser Ile Arg Ser Ser Ile Leu Ala		
[2619]	340	345	350
[2620]	Asp Leu Phe Asp Ser Gln Val Val Asp Gly Thr Thr Glu Asp Ala Asn		
[2621]	355	360	365
[2622]	Gly Asn Lys Val Asn Thr Lys Val Met Leu Ser Met Gln Asp Phe Gly		
[2623]	370	375	380
[2624]	Leu Ser Leu Asn Asp Ala Gly Thr Leu Ser Phe Asp Ser Ser Lys Phe		
[2625]	385	390	395
[2626]	Glu Gln Lys Val Lys Glu Asp Pro Asp Ser Thr Glu Ser Phe Phe Ser		
[2627]	405	410	415
[2628]	Asn Ile Thr Lys Tyr Glu Asp Ile Asn His Thr Gly Glu Val Ile Lys		
[2629]	420	425	430
[2630]	Thr Gly Ser Leu Ser Lys Tyr Leu Asn Ser Asn Gly Gly Asn Thr Asn		
[2631]	435	440	445
[2632]	Gly Leu Glu Phe Lys Pro Gly Asp Phe Thr Ile Val Phe Asn Asn Gln		
[2633]	450	455	460
[2634]	Thr Tyr Asp Leu Ser Lys Asn Ser Asp Gly Thr Asn Phe Lys Leu Thr		
[2635]	465	470	475
[2636]	Gly Lys Thr Glu Glu Glu Leu Leu Gln Asn Leu Ala Asn His Ile Asn		
[2637]	485	490	495
[2638]	Ser Lys Gly Ile Glu Gly Leu Lys Val Lys Val Glu Ser Tyr Asn Gln		
[2639]	500	505	510

[2640]	Asn Asn Val Thr Gly Phe Arg Leu Asn Phe Ser Gly Asp Gly Ser Ser
[2641]	515 520 525
[2642]	Asp Phe Ser Ile Lys Gly Asp Ala Asn Ile Leu Lys Glu Leu Gly Leu
[2643]	530 535 540
[2644]	Ser Asp Val Asn Ile Thr Ser Lys Pro Ile Glu Gly Lys Gly Ile Phe
[2645]	545 550 555 560
[2646]	Ser Lys Leu Lys Ala Thr Leu Gln Glu Met Thr Gly Lys Asp Gly Ser
[2647]	565 570 575
[2648]	Ile Thr Lys Tyr Asp Glu Ser Leu Thr Asn Asp Ile Lys Ser Leu Asn
[2649]	580 585 590
[2650]	Thr Ser Lys Asp Ser Thr Gln Ala Met Ile Asp Thr Arg Tyr Asp Thr
[2651]	595 600 605
[2652]	Met Ala Asn Gln Trp Leu Gln Tyr Glu Ser Ile Leu Asn Lys Leu Asn
[2653]	610 615 620
[2654]	Gln Gln Leu Asn Thr Val Thr Asn Met Ile Asn Ala Ala Asn Asn Ser
[2655]	625 630 635 640
[2656]	Asn Asn
[2657]	<210> 66
[2658]	<211> 642
[2659]	<212> PRT
[2660]	<213> 人工序列(Artificial Sequence)
[2661]	<220>
[2662]	<223> 合成序列- 鞭毛钩相关
[2663]	蛋白Flid [空肠弯曲杆菌4031] GenBank:
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[2668]	Thr Gln Asp Thr Ile Asp Lys Leu Lys Glu Ala Glu Gln Lys Ala Arg
[2669]	20 25 30
[2670]	Ile Asp Pro Tyr Thr Lys Lys Ile Glu Glu Asn Thr Thr Lys Gln Lys
[2671]	35 40 45
[2672]	Asp Leu Thr Glu Ile Lys Thr Lys Leu Leu Ser Phe Gln Thr Ala Val
[2673]	50 55 60
[2674]	Ser Ser Leu Ala Asp Ala Thr Val Phe Ala Lys Arg Lys Val Val Gly
[2675]	65 70 75 80
[2676]	Ser Ile Ser Asp Asn Pro Pro Ala Ser Leu Thr Val Asn Ser Gly Val
[2677]	85 90 95
[2678]	Ala Leu Gln Ser Met Asn Ile Asn Val Thr Gln Leu Ala Gln Lys Asp

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[2680]	Val	Tyr	Gln	Ser	Gln	Gly	Leu	Ala	Asn	Asp	Gly	Gly	Phe	Val	Asn	Ala				
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[2682]	Lys	Leu	Asn	Gly	Thr	Ala	Asp	Leu	Thr	Phe	Phe	Ser	Asn	Gly	Lys	Glu				
[2683]			130						135				140							
[2684]	Tyr	Thr	Val	Thr	Val	Asp	Lys	Asn	Thr	Thr	Tyr	Arg	Asp	Leu	Ala	Asp				
[2685]			145						150				155							160
[2686]	Lys	Ile	Asn	Glu	Ala	Ser	Gly	Gly	Glu	Ile	Val	Ala	Lys	Ile	Val	Asn				
[2687]									165											175
[2688]	Thr	Gly	Glu	Lys	Gly	Thr	Pro	Tyr	Arg	Leu	Thr	Leu	Thr	Ser	Lys	Glu				
[2689]									180											190
[2690]	Thr	Gly	Glu	Asp	Ser	Ala	Ile	Ser	Phe	Tyr	Ala	Gly	Lys	Lys	Asp	Ala				
[2691]									195											205
[2692]	Gln	Gly	Gln	Tyr	Lys	Ser	Asp	Ser	Glu	Ala	Glu	Lys	Ile	Phe	Lys	Ser				
[2693]									210											220
[2694]	Leu	Gly	Trp	Glu	Leu	Asp	Thr	Thr	Ser	Ser	Ile	Asp	Pro	Ala	Lys	Asp				
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[2696]	Lys	Lys	Gly	Tyr	Gly	Ile	Lys	Asp	Ala	Ser	Leu	His	Ile	Gln	Thr	Ala				
[2697]									245											255
[2698]	Gln	Asn	Ala	Glu	Phe	Thr	Leu	Asp	Gly	Ile	Lys	Met	Phe	Arg	Ser	Ser				
[2699]									260											270
[2700]	Asn	Thr	Val	Thr	Asp	Leu	Gly	Val	Gly	Met	Thr	Leu	Thr	Leu	Asn	Lys				
[2701]									275											285
[2702]	Thr	Gly	Glu	Ile	Asn	Phe	Asp	Val	Gln	Gln	Asp	Phe	Glu	Gly	Val	Thr				
[2703]									290											300
[2704]	Lys	Ala	Met	Gln	Asp	Leu	Val	Asp	Ala	Tyr	Asn	Asp	Leu	Val	Thr	Asn				
[2705]									305											320
[2706]	Leu	Asn	Ala	Ala	Thr	Asp	Tyr	Asn	Ser	Glu	Thr	Gly	Thr	Lys	Gly	Thr				
[2707]									325											335
[2708]	Leu	Gln	Gly	Ile	Ser	Glu	Val	Asn	Ser	Ile	Arg	Ser	Ser	Ile	Leu	Ala				
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[2710]	Asp	Leu	Phe	Asp	Ser	Gln	Val	Val	Asp	Gly	Thr	Thr	Glu	Asp	Ala	Asn				
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[2712]	Gly	Asn	Lys	Val	Asn	Thr	Lys	Val	Met	Leu	Ser	Met	Gln	Asp	Phe	Gly				
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[2714]	Leu	Ser	Leu	Asn	Asp	Ala	Gly	Thr	Leu	Ser	Phe	Asp	Ser	Ser	Lys	Phe				
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[2716]	Glu	Gln	Lys	Val	Lys	Glu	Asp	Pro	Asp	Ser	Thr	Glu	Ser	Phe	Phe	Ser				
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[2718]	Asn Ile Thr Lys Tyr Glu Asp Ile Asn His Thr Gly Glu Val Ile Lys
[2719]	420 425 430
[2720]	Thr Gly Ser Leu Ser Lys Tyr Leu Asn Ser Asn Gly Gly Asn Thr Asn
[2721]	435 440 445
[2722]	Gly Leu Glu Phe Lys Pro Gly Asp Phe Thr Ile Val Phe Asn Asn Gln
[2723]	450 455 460
[2724]	Thr Tyr Asp Leu Ser Lys Asn Ser Asp Gly Thr Asn Phe Lys Leu Thr
[2725]	465 470 475 480
[2726]	Gly Lys Thr Glu Glu Glu Leu Leu Gln Asn Leu Ala Asn His Ile Asn
[2727]	485 490 495
[2728]	Ser Lys Gly Ile Glu Gly Leu Lys Val Lys Val Glu Ser Tyr Asn Gln
[2729]	500 505 510
[2730]	Asn Asn Val Thr Gly Phe Arg Leu Asn Phe Ser Gly Asp Gly Ser Ser
[2731]	515 520 525
[2732]	Asp Phe Ser Ile Lys Gly Asp Ala Asn Ile Leu Lys Glu Leu Gly Leu
[2733]	530 535 540
[2734]	Ser Asp Val Asn Ile Thr Ser Lys Pro Ile Glu Gly Lys Gly Ile Phe
[2735]	545 550 555 560
[2736]	Ser Lys Leu Lys Ala Thr Leu Gln Glu Met Thr Gly Lys Asp Gly Ser
[2737]	565 570 575
[2738]	Ile Thr Lys Tyr Asp Glu Ser Leu Thr Asn Asp Ile Lys Ser Leu Asn
[2739]	580 585 590
[2740]	Thr Ser Lys Asp Ser Thr Gln Ala Met Ile Asp Thr Arg Tyr Asp Thr
[2741]	595 600 605
[2742]	Met Ala Asn Gln Trp Leu Gln Tyr Glu Ser Ile Leu Asn Lys Leu Asn
[2743]	610 615 620
[2744]	Gln Gln Leu Asn Thr Val Thr Asn Met Ile Asn Ala Ala Asn Asn Ser
[2745]	625 630 635 640
[2746]	Asn Asn
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[2748]	<211> 643
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[2752]	<223> 合成序列-鞭毛钩相关
[2753]	蛋白2 [空肠弯曲杆菌亚种空肠M1]
[2754]	GenBank: ADN90737.1
[2755]	<400> 67
[2756]	Met Ala Phe Gly Ser Leu Ser Ser Leu Gly Phe Gly Ser Gly Val Leu

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[2760]	Ile Asp Pro Tyr Thr Lys Lys Ile Glu Glu Asn Thr Thr Lys Gln Lys			
[2761]		35	40	45
[2762]	Asp Leu Thr Glu Ile Lys Thr Lys Leu Leu Ser Phe Gln Thr Ala Val			
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[2764]	Ser Ser Leu Ala Asp Ala Thr Val Phe Ala Lys Arg Lys Val Val Gly			
[2765]		65	70	75
[2766]	Ser Ile Ser Asp Asn Pro Pro Ala Ser Leu Thr Val Asn Ser Gly Val			
[2767]		85	90	95
[2768]	Ala Leu Gln Ser Met Asn Ile Asn Val Thr Gln Leu Ala Gln Lys Asp			
[2769]		100	105	110
[2770]	Val Tyr Gln Ser Lys Gly Leu Ala Asn Asp Ser Gly Phe Val Asn Ala			
[2771]		115	120	125
[2772]	Asn Leu Thr Gly Thr Thr Asp Leu Thr Phe Phe Ser Asn Gly Lys Glu			
[2773]		130	135	140
[2774]	Tyr Thr Val Thr Val Asp Lys Asn Thr Thr Tyr Arg Asp Leu Ala Asp			
[2775]		145	150	155
[2776]	Lys Ile Asn Glu Ala Ser Gly Gly Glu Ile Val Ala Lys Ile Val Asn			
[2777]		165	170	175
[2778]	Thr Gly Glu Lys Gly Thr Pro Tyr Arg Leu Thr Leu Thr Ser Lys Glu			
[2779]		180	185	190
[2780]	Thr Gly Glu Asp Ser Ala Ile Ser Phe Tyr Ala Gly Lys Lys Asp Ala			
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[2782]	Gln Gly Gln Tyr Gln Ser Asp Pro Glu Ala Glu Asn Ile Phe Ser Asn			
[2783]		210	215	220
[2784]	Leu Gly Trp Glu Leu Asp Lys Thr Thr Gln Thr Ile Asp Pro Ala Lys			
[2785]		225	230	235
[2786]	Asp Lys Lys Gly Tyr Gly Ile Lys Asp Ala Ser Leu His Ile Gln Thr			
[2787]		245	250	255
[2788]	Ala Gln Asn Ala Glu Phe Thr Leu Asp Gly Ile Lys Met Phe Arg Ser			
[2789]		260	265	270
[2790]	Ser Asn Thr Val Thr Asp Leu Gly Val Gly Met Thr Leu Thr Leu Asn			
[2791]		275	280	285
[2792]	Lys Thr Gly Glu Ile Asn Phe Asp Val Gln Gln Asp Phe Glu Gly Val			
[2793]		290	295	300
[2794]	Thr Lys Ala Met Gln Asp Leu Val Asp Ala Tyr Asn Asp Leu Val Thr			
[2795]		305	310	315
				320

[2796]	Asn Leu Asn Ala Ala Thr Asp Tyr Asn Ser Glu Thr Gly Thr Lys Gly
[2797]	325 330 335
[2798]	Thr Leu Gln Gly Ile Ser Glu Val Asn Ser Ile Arg Ser Ser Ile Leu
[2799]	340 345 350
[2800]	Ala Asp Leu Phe Asp Ser Gln Val Val Asp Gly Thr Thr Glu Asp Ala
[2801]	355 360 365
[2802]	Asn Gly Asn Lys Val Asn Thr Lys Val Met Leu Ser Met Gln Asp Phe
[2803]	370 375 380
[2804]	Gly Leu Ser Leu Asn Asp Ala Gly Thr Leu Ser Phe Asp Ser Ser Lys
[2805]	385 390 395 400
[2806]	Phe Glu Gln Lys Val Lys Glu Asp Pro Asp Ser Thr Glu Ser Phe Phe
[2807]	405 410 415
[2808]	Ser Asn Ile Thr Lys Tyr Glu Asp Ile Asn His Thr Gly Glu Val Ile
[2809]	420 425 430
[2810]	Lys Gln Gly Ser Leu Asn Gln Tyr Leu Asp Ser Ser Gly Thr Gly Asn
[2811]	435 440 445
[2812]	Lys Gly Leu Asp Phe Lys Pro Gly Asp Phe Thr Ile Val Phe Asn Asn
[2813]	450 455 460
[2814]	Gln Thr Tyr Asp Leu Ser Lys Asn Ser Asp Gly Thr Asn Phe Lys Leu
[2815]	465 470 475 480
[2816]	Thr Gly Lys Thr Glu Glu Glu Leu Leu Gln Asn Leu Ala Asn His Ile
[2817]	485 490 495
[2818]	Asn Ser Lys Gly Ile Glu Gly Leu Lys Val Lys Val Glu Ser Tyr Asp
[2819]	500 505 510
[2820]	Gln Asn Gly Val Lys Gly Phe Lys Leu Asn Phe Ser Gly Asp Gly Ser
[2821]	515 520 525
[2822]	Ser Asp Phe Ser Ile Lys Gly Asn Ala Thr Ile Leu Gln Glu Leu Gly
[2823]	530 535 540
[2824]	Leu Ser Asp Val Asn Ile Thr Ser Lys Pro Ile Glu Gly Lys Gly Ile
[2825]	545 550 555 560
[2826]	Phe Ser Lys Leu Lys Ala Thr Leu Gln Glu Met Thr Gly Lys Asp Gly
[2827]	565 570 575
[2828]	Ser Ile Thr Lys Tyr Asp Glu Ser Leu Thr Asn Asp Ile Lys Ser Leu
[2829]	580 585 590
[2830]	Asn Thr Ser Lys Asp Ser Thr Gln Ala Met Ile Asp Thr Arg Tyr Asp
[2831]	595 600 605
[2832]	Thr Met Ala Asn Gln Trp Leu Gln Tyr Glu Ser Ile Leu Asn Lys Leu
[2833]	610 615 620
[2834]	Asn Gln Gln Leu Asn Thr Val Thr Asn Met Ile Asn Ala Ala Asn Asn

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[2836]	Ser Asn Asn			
[2837]	<210> 68			
[2838]	<211> 643			
[2839]	<212> PRT			
[2840]	<213> 人工序列(Artificial Sequence)			
[2841]	<220>			
[2842]	<223> 合成序列-鞭毛丝加帽			
[2843]	蛋白FliD [空肠弯曲杆菌亚种空肠菌株RM3420]			
[2844]	GenBank: A0W96893.1			
[2845]	<400> 68			
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[2849]		20	25	30
[2850]	Ile Asp Pro Tyr Thr Lys Lys Ile Glu Glu Asn Thr Thr Lys Gln Lys			
[2851]		35	40	45
[2852]	Asp Leu Thr Glu Ile Lys Thr Lys Leu Leu Ser Phe Gln Thr Ala Val			
[2853]		50	55	60
[2854]	Ser Ser Leu Ala Asp Ala Thr Val Phe Ala Lys Arg Lys Val Val Gly			
[2855]		65	70	75
[2856]	Ser Ile Ser Asp Asn Pro Pro Ala Ser Leu Thr Val Asn Ser Gly Val			
[2857]		85	90	95
[2858]	Ala Leu Gln Ser Met Asn Ile Asn Val Thr Gln Leu Ala Gln Lys Asp			
[2859]		100	105	110
[2860]	Val Tyr Gln Ser Lys Gly Leu Ala Asn Asp Ser Gly Phe Ile Asn Ala			
[2861]		115	120	125
[2862]	Asn Leu Thr Gly Thr Thr Asp Leu Thr Phe Phe Ser Asn Gly Lys Glu			
[2863]		130	135	140
[2864]	Tyr Thr Val Thr Val Asp Lys Ser Thr Thr Tyr Arg Asp Leu Ala Asp			
[2865]		145	150	155
[2866]	Lys Ile Asn Glu Ala Ser Gly Gly Glu Ile Val Ala Lys Ile Val Asn			
[2867]		165	170	175
[2868]	Thr Gly Glu Lys Gly Thr Pro Tyr Arg Leu Thr Leu Thr Ser Lys Glu			
[2869]		180	185	190
[2870]	Thr Gly Glu Asp Ser Ala Ile Ser Phe Tyr Ala Gly Lys Lys Asp Ala			
[2871]		195	200	205
[2872]	Gln Gly Gln Tyr Lys Ser Asp Ser Glu Ala Glu Lys Ile Phe Ser Asn			
[2873]		210	215	220

[2874]	Leu Gly Trp Glu Leu Asp Lys Thr Thr Gln Thr Ile Asp Pro Ala Lys
[2875]	225 230 235 240
[2876]	Asp Lys Lys Gly Tyr Gly Ile Lys Asp Ala Ser Leu His Ile Gln Thr
[2877]	245 250 255
[2878]	Ala Gln Asn Ala Glu Phe Thr Leu Asp Gly Ile Lys Met Phe Arg Ser
[2879]	260 265 270
[2880]	Ser Asn Thr Val Thr Asp Leu Gly Val Gly Met Thr Leu Thr Leu Asn
[2881]	275 280 285
[2882]	Lys Thr Gly Glu Ile Asn Phe Asp Val Gln Gln Asp Phe Glu Gly Val
[2883]	290 295 300
[2884]	Thr Lys Ala Met Gln Asp Leu Val Asp Ala Tyr Asn Asp Leu Val Thr
[2885]	305 310 315 320
[2886]	Asn Leu Asn Ala Ala Thr Asp Tyr Asn Ser Glu Thr Gly Thr Lys Gly
[2887]	325 330 335
[2888]	Thr Leu Gln Gly Ile Ser Glu Val Asn Ser Ile Arg Ser Ser Ile Leu
[2889]	340 345 350
[2890]	Ala Asp Leu Phe Asp Ser Gln Val Val Asp Gly Thr Thr Glu Asp Ala
[2891]	355 360 365
[2892]	Asn Gly Asn Lys Val Asn Thr Lys Val Met Leu Ser Met Gln Asp Phe
[2893]	370 375 380
[2894]	Gly Leu Ser Leu Asn Asp Ala Gly Thr Leu Ser Phe Asp Ser Ser Lys
[2895]	385 390 395 400
[2896]	Phe Glu Gln Lys Val Lys Glu Asp Pro Asp Ser Thr Glu Ser Phe Phe
[2897]	405 410 415
[2898]	Ser Asn Ile Thr Lys Tyr Glu Asp Ile Asn His Thr Gly Glu Val Ile
[2899]	420 425 430
[2900]	Lys Gln Gly Ser Leu Asn Gln Tyr Leu Asp Ser Ser Gly Thr Gly Asn
[2901]	435 440 445
[2902]	Lys Gly Leu Glu Phe Lys Pro Gly Gly Phe Thr Ile Val Phe Asn Asn
[2903]	450 455 460
[2904]	Gln Thr Tyr Asp Leu Ser Lys Asn Ser Asp Gly Thr Asn Phe Lys Leu
[2905]	465 470 475 480
[2906]	Thr Gly Lys Thr Glu Glu Glu Leu Leu Gln Asn Leu Ala Asn His Ile
[2907]	485 490 495
[2908]	Asn Ser Lys Gly Ile Glu Gly Leu Lys Val Lys Val Glu Ser Tyr Asp
[2909]	500 505 510
[2910]	Gln Asn Gly Val Lys Gly Phe Lys Leu Lys Phe Ser Gly Asp Gly Ser
[2911]	515 520 525
[2912]	Ser Asp Phe Ser Ile Lys Gly Asp Ala Asn Ile Leu Lys Glu Leu Gly

[2913]	530	535	540
[2914]	Leu Ser Asp Val Asn Ile Thr Ser Lys Pro Ile Glu Gly Lys Gly Ile		
[2915]	545	550	555
[2916]	Phe Ser Lys Leu Lys Ala Thr Leu Gln Glu Met Thr Gly Lys Asp Gly		
[2917]	565	570	575
[2918]	Ser Ile Thr Lys Tyr Asp Glu Ser Leu Thr Asn Asp Ile Lys Ser Leu		
[2919]	580	585	590
[2920]	Asn Thr Ser Lys Asp Ser Thr Gln Ala Met Ile Asp Thr Arg Tyr Asp		
[2921]	595	600	605
[2922]	Thr Met Ala Asn Gln Trp Leu Gln Tyr Glu Ser Ile Leu Asn Lys Leu		
[2923]	610	615	620
[2924]	Asn Gln Gln Leu Asn Thr Val Thr Asn Met Ile Asn Ala Ala Asn Asn		
[2925]	625	630	635
[2926]	Ser Asn Asn		
[2927]	<210> 69		
[2928]	<211> 642		
[2929]	<212> PRT		
[2930]	<213> 人工序列(Artificial Sequence)		
[2931]	<220>		
[2932]	<223> 合成序列-鞭毛丝加帽		
[2933]	蛋白F1iD [空肠弯曲杆菌亚种空肠]		
[2934]	GenBank: AON66729.1		
[2935]	<400> 69		
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[2939]	20	25	30
[2940]	Ile Asp Pro Tyr Thr Lys Lys Ile Glu Glu Asn Thr Thr Lys Gln Lys		
[2941]	35	40	45
[2942]	Asp Leu Thr Glu Ile Lys Thr Lys Leu Leu Ser Phe Gln Thr Ala Val		
[2943]	50	55	60
[2944]	Ser Ser Leu Ala Asp Ala Thr Val Phe Ala Lys Arg Lys Val Val Gly		
[2945]	65	70	75
[2946]	Ser Ile Ser Asp Asn Pro Pro Ala Ser Leu Thr Val Asn Ser Gly Val		
[2947]	85	90	95
[2948]	Ala Leu Gln Ser Met Asn Ile Asn Val Thr Gln Leu Ala Gln Lys Asp		
[2949]	100	105	110
[2950]	Val Tyr Gln Ser Gln Gly Leu Ala Asn Asp Gly Gly Phe Val Asn Ala		
[2951]	115	120	125

[2952]	Lys Leu Asn Gly Thr Ala Asp Leu Thr Phe Phe Ser Asn Gly Lys Glu
[2953]	130 135 140
[2954]	Tyr Thr Val Thr Val Asp Lys Asn Thr Thr Tyr Arg Asp Leu Ala Asp
[2955]	145 150 155 160
[2956]	Lys Ile Asn Glu Ala Ser Gly Gly Glu Ile Val Ala Lys Ile Val Asn
[2957]	165 170 175
[2958]	Thr Gly Glu Lys Gly Thr Pro Tyr Arg Leu Thr Leu Thr Ser Lys Glu
[2959]	180 185 190
[2960]	Thr Gly Glu Asp Ser Ala Ile Ser Phe Tyr Ala Gly Lys Lys Asp Ala
[2961]	195 200 205
[2962]	Gln Gly Gln Tyr Lys Ser Asp Pro Glu Ala Glu Lys Ile Phe Lys Ser
[2963]	210 215 220
[2964]	Leu Gly Trp Glu Leu Asp Thr Thr Ser Ser Ile Asp Pro Ala Lys Asp
[2965]	225 230 235 240
[2966]	Lys Lys Gly Tyr Gly Ile Lys Asp Ala Ser Leu His Ile Gln Thr Ala
[2967]	245 250 255
[2968]	Gln Asn Ala Glu Phe Thr Leu Asp Gly Ile Lys Met Phe Arg Ser Ser
[2969]	260 265 270
[2970]	Asn Thr Val Thr Asp Leu Gly Val Gly Met Thr Leu Thr Leu Asn Lys
[2971]	275 280 285
[2972]	Thr Gly Glu Ile Asn Phe Asp Val Gln Gln Asp Phe Glu Gly Val Thr
[2973]	290 295 300
[2974]	Lys Ala Met Gln Asp Leu Val Asp Ala Tyr Asn Asp Leu Val Thr Asn
[2975]	305 310 315 320
[2976]	Leu Asn Ala Ala Thr Asp Tyr Asn Ser Glu Thr Gly Ile Lys Gly Thr
[2977]	325 330 335
[2978]	Leu Gln Gly Ile Ser Glu Val Asn Ser Ile Arg Ser Ser Ile Leu Ala
[2979]	340 345 350
[2980]	Asp Leu Phe Asp Ser Gln Val Val Asp Gly Thr Thr Glu Asp Ala Asn
[2981]	355 360 365
[2982]	Gly Asn Lys Val Asn Thr Lys Val Met Leu Ser Met Gln Asp Phe Gly
[2983]	370 375 380
[2984]	Leu Ser Leu Asn Asp Ala Gly Thr Leu Ser Phe Asp Ser Ser Lys Phe
[2985]	385 390 395 400
[2986]	Glu Gln Lys Val Lys Glu Asp Pro Asp Ser Thr Glu Ser Phe Phe Ser
[2987]	405 410 415
[2988]	Asn Ile Thr Lys Tyr Glu Asp Ile Asn His Thr Gly Glu Val Ile Lys
[2989]	420 425 430
[2990]	Thr Gly Ser Leu Ser Lys Tyr Leu Asn Ser Asn Gly Gly Asn Thr Asn

[2991]	435	440	445
[2992]	Gly Leu Glu Phe Lys Pro Gly Asp Phe Thr Ile Val Phe Asn Asn Gln		
[2993]	450	455	460
[2994]	Thr Tyr Asp Leu Ser Lys Asn Ser Asp Gly Thr Asn Phe Lys Leu Thr		
[2995]	465	470	475
[2996]	Gly Lys Thr Glu Glu Glu Leu Leu Gln Asn Leu Ala Asn His Ile Asn		
[2997]	485	490	495
[2998]	Ser Lys Gly Ile Glu Gly Leu Lys Val Lys Val Glu Ser Tyr Asn Gln		
[2999]	500	505	510
[3000]	Asn Asn Val Thr Gly Phe Arg Leu Asn Phe Ser Gly Asp Gly Ser Ser		
[3001]	515	520	525
[3002]	Asp Phe Ser Ile Lys Gly Asp Ala Asn Ile Leu Lys Glu Leu Gly Leu		
[3003]	530	535	540
[3004]	Ser Asp Val Asn Ile Thr Ser Lys Pro Ile Glu Gly Lys Gly Ile Phe		
[3005]	545	550	555
[3006]	Ser Lys Leu Lys Ala Thr Leu Gln Glu Met Thr Gly Lys Asp Gly Ser		
[3007]	565	570	575
[3008]	Ile Thr Lys Tyr Asp Glu Ser Leu Thr Asn Asp Ile Lys Ser Leu Asn		
[3009]	580	585	590
[3010]	Thr Ser Lys Asp Ser Thr Gln Ala Met Ile Asp Thr Arg Tyr Asp Thr		
[3011]	595	600	605
[3012]	Met Ala Asn Gln Trp Leu Gln Tyr Glu Ser Ile Leu Asn Lys Leu Asn		
[3013]	610	615	620
[3014]	Gln Gln Leu Asn Thr Val Thr Asn Met Ile Asn Ala Ala Asn Asn Ser		
[3015]	625	630	635
[3016]	Asn Asn		
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[3024]	GenBank: AON65179.1		
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[3029]	20	25	30

[3030]	Ile Asp Pro Tyr Thr Lys Lys Ile Glu Glu Asn Thr Thr Lys Gln Lys
[3031]	35 40 45
[3032]	Asp Leu Thr Glu Ile Lys Thr Lys Leu Leu Ser Phe Gln Thr Ala Val
[3033]	50 55 60
[3034]	Ser Ser Leu Ala Asp Ala Thr Val Phe Ala Lys Arg Lys Val Val Gly
[3035]	65 70 75 80
[3036]	Ser Ile Ser Asp Asn Pro Pro Ala Ser Leu Thr Val Asn Ser Gly Val
[3037]	85 90 95
[3038]	Ala Leu Gln Ser Met Asn Ile Asn Val Thr Gln Leu Ala Gln Lys Asp
[3039]	100 105 110
[3040]	Val Tyr Gln Ser Gln Gly Leu Ala Asn Asp Ser Gly Phe Ile Asn Ala
[3041]	115 120 125
[3042]	Asn Leu Ala Gly Thr Thr Asp Leu Thr Phe Phe Ser Asn Gly Lys Glu
[3043]	130 135 140
[3044]	Tyr Thr Val Thr Val Asp Lys Asn Thr Thr Tyr Arg Asp Leu Ala Asp
[3045]	145 150 155 160
[3046]	Lys Ile Asn Glu Ala Ser Gly Gly Glu Ile Val Ala Lys Ile Val Asn
[3047]	165 170 175
[3048]	Thr Gly Glu Lys Gly Thr Pro Tyr Arg Leu Thr Leu Thr Ser Lys Glu
[3049]	180 185 190
[3050]	Thr Gly Glu Asp Ser Ala Ile Ser Phe Tyr Ala Gly Lys Lys Asp Ala
[3051]	195 200 205
[3052]	Gln Gly Gln Tyr Gln Ser Asp Pro Glu Ala Glu Lys Ile Phe Ser Asn
[3053]	210 215 220
[3054]	Leu Gly Trp Glu Leu Asp Lys Thr Thr Gln Thr Ile Asp Pro Ala Lys
[3055]	225 230 235 240
[3056]	Asp Lys Lys Gly Tyr Gly Ile Lys Asp Ala Ser Leu His Ile Gln Thr
[3057]	245 250 255
[3058]	Ala Gln Asn Ala Glu Phe Thr Leu Asp Gly Ile Lys Met Phe Arg Ser
[3059]	260 265 270
[3060]	Ser Asn Thr Val Thr Asp Leu Gly Val Gly Met Thr Leu Thr Leu Asn
[3061]	275 280 285
[3062]	Lys Thr Gly Glu Ile Asn Phe Asp Val Gln Gln Asp Phe Glu Gly Val
[3063]	290 295 300
[3064]	Thr Lys Ala Met Gln Asp Leu Val Asp Ala Tyr Asn Asp Leu Val Thr
[3065]	305 310 315 320
[3066]	Asn Leu Asn Ala Ala Thr Asp Tyr Asn Ser Glu Thr Gly Thr Lys Gly
[3067]	325 330 335
[3068]	Thr Leu Gln Gly Ile Ser Glu Val Asn Ser Ile Arg Ser Ser Ile Leu

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[3070]	Ala	Asp	Leu	Phe	Asp	Ser	Gln	Val	Val	Asp	Gly	Thr	Thr	Glu	Asp	Ala			
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[3072]	Asn	Gly	Asn	Lys	Val	Asn	Thr	Lys	Val	Met	Leu	Ser	Met	Gln	Asp	Phe			
[3073]			370					375						380					
[3074]	Gly	Leu	Ser	Leu	Asn	Asp	Ala	Gly	Thr	Leu	Ser	Phe	Asp	Ser	Ser	Lys			
[3075]			385					390						395					400
[3076]	Phe	Glu	Gln	Lys	Val	Lys	Glu	Asp	Pro	Asp	Ser	Thr	Glu	Ser	Phe	Phe			
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[3078]	Ser	Asn	Ile	Thr	Lys	Tyr	Glu	Asp	Ile	Asn	His	Thr	Gly	Glu	Val	Ile			
[3079]					420														430
[3080]	Lys	Thr	Gly	Ser	Leu	Ser	Lys	Tyr	Leu	Asn	Ser	Asn	Gly	Gly	Asn	Thr			
[3081]					435														445
[3082]	Asn	Gly	Leu	Ala	Phe	Lys	Pro	Gly	Asp	Phe	Thr	Ile	Val	Phe	Asn	Asn			
[3083]					450														460
[3084]	Gln	Thr	Tyr	Asp	Leu	Ser	Lys	Asn	Ser	Asp	Gly	Thr	Asn	Phe	Lys	Leu			
[3085]					465														480
[3086]	Thr	Gly	Lys	Thr	Glu	Glu	Glu	Leu	Leu	Gln	Asn	Leu	Ala	Asn	His	Ile			
[3087]					485														495
[3088]	Asn	Ser	Lys	Gly	Ile	Glu	Gly	Leu	Lys	Val	Lys	Val	Glu	Ser	Tyr	Asn			
[3089]					500														510
[3090]	Gln	Asn	Asn	Val	Thr	Gly	Phe	Arg	Leu	Asn	Phe	Ser	Gly	Asp	Gly	Ser			
[3091]					515														525
[3092]	Ser	Asp	Phe	Ser	Ile	Lys	Gly	Asp	Gly	Ser	Ile	Leu	Lys	Glu	Leu	Gly			
[3093]					530														540
[3094]	Leu	Ser	Asp	Val	Asn	Ile	Thr	Ser	Lys	Pro	Ile	Glu	Gly	Lys	Gly	Ile			
[3095]					545														560
[3096]	Phe	Ser	Lys	Leu	Lys	Ala	Thr	Leu	Gln	Glu	Met	Thr	Gly	Lys	Asp	Gly			
[3097]					565														575
[3098]	Ser	Ile	Thr	Lys	Tyr	Asp	Glu	Ser	Leu	Thr	Asn	Asp	Ile	Lys	Ser	Leu			
[3099]					580														590
[3100]	Asn	Thr	Ser	Lys	Asp	Ser	Thr	Gln	Ala	Met	Ile	Asp	Thr	Arg	Tyr	Asp			
[3101]					595														605
[3102]	Thr	Met	Ala	Asn	Gln	Trp	Leu	Gln	Tyr	Glu	Ser	Ile	Leu	Asn	Lys	Leu			
[3103]					610														620
[3104]	Asn	Gln	Gln	Leu	Asn	Thr	Val	Thr	Asn	Met	Ile	Asn	Ala	Ala	Asn	Asn			
[3105]					625														640
[3106]	Ser	Asn	Asn																
[3107]	<210>	71																	

[3108] <211> 637
 [3109] <212> PRT
 [3110] <213> 人工序列(Artificial Sequence)
 [3111] <220>
 [3112] <223> 合成序列-鞭毛丝加帽
 [3113] 蛋白[空肠弯曲杆菌亚种空肠]
 [3114] GenBank: A0H51565.1
 [3115] <400> 71
 [3116] Met Ala Phe Gly Ser Leu Ser Ser Leu Gly Phe Gly Ser Gly Val Leu
 [3117] 1 5 10 15
 [3118] Thr Gln Asp Thr Ile Asp Lys Leu Lys Glu Ala Glu Gln Lys Ala Arg
 [3119] 20 25 30
 [3120] Ile Asp Pro Tyr Thr Lys Lys Ile Glu Glu Asn Thr Thr Lys Gln Lys
 [3121] 35 40 45
 [3122] Asp Leu Thr Glu Ile Lys Thr Lys Leu Leu Ser Phe Gln Thr Ala Val
 [3123] 50 55 60
 [3124] Ser Ser Leu Ala Asp Ala Thr Val Phe Ala Lys Arg Lys Val Val Gly
 [3125] 65 70 75 80
 [3126] Ser Ile Ser Asp Asn Pro Pro Ala Ser Leu Thr Val Asn Ser Gly Val
 [3127] 85 90 95
 [3128] Ala Leu Gln Ser Met Asn Ile Asn Val Thr Gln Leu Ala Gln Lys Asp
 [3129] 100 105 110
 [3130] Val Tyr Gln Ser Lys Gly Leu Ala Asn Asp Gly Gly Phe Val Asn Ala
 [3131] 115 120 125
 [3132] Gln Leu Asn Gly Thr Ala Asp Leu Thr Phe Phe Ser Asn Gly Lys Glu
 [3133] 130 135 140
 [3134] Tyr Thr Val Thr Val Asp Lys Asn Thr Thr Tyr Arg Asp Leu Ala Asp
 [3135] 145 150 155 160
 [3136] Lys Ile Asn Glu Ala Ser Gly Gly Glu Ile Val Ala Lys Ile Val Asn
 [3137] 165 170 175
 [3138] Thr Gly Glu Lys Gly Thr Pro Tyr Arg Leu Thr Leu Thr Ser Lys Glu
 [3139] 180 185 190
 [3140] Thr Gly Glu Asp Ser Ala Ile Ser Phe Tyr Ala Gly Lys Lys Asp Ser
 [3141] 195 200 205
 [3142] Asn Gly Gln Tyr Gln Ser Asp Ser Glu Ala Glu Asn Ile Phe Ser Asn
 [3143] 210 215 220
 [3144] Leu Gly Trp Glu Leu Asp Lys Thr Ser Ser Ile Asp Pro Ala Lys Asp
 [3145] 225 230 235 240
 [3146] Lys Lys Gly Tyr Gly Ile Lys Asp Ala Ser Leu His Ile Gln Thr Ala

[3147]		245		250		255
[3148]	Gln Asn Ala Glu Phe Thr Leu Asp Gly Ile Lys Met Phe Arg Ser Ser					
[3149]		260		265		270
[3150]	Asn Thr Val Thr Asp Leu Gly Val Gly Met Thr Leu Thr Leu Asn Lys					
[3151]		275		280		285
[3152]	Thr Gly Glu Ile Asn Phe Asp Val Gln Gln Asp Phe Glu Gly Val Thr					
[3153]		290		295		300
[3154]	Lys Ala Met Gln Asp Leu Val Asp Ala Tyr Asn Asp Leu Val Thr Asn					
[3155]		305		310		315
[3156]	Leu Asn Ala Ala Thr Asp Tyr Asn Ser Glu Thr Gly Thr Lys Gly Thr					
[3157]		325		330		335
[3158]	Leu Gln Gly Ile Ser Glu Val Asn Ser Ile Arg Ser Ser Ile Leu Ala					
[3159]		340		345		350
[3160]	Asp Leu Phe Asp Ser Gln Val Val Asp Gly Thr Thr Glu Asp Ala Asn					
[3161]		355		360		365
[3162]	Gly Asn Lys Val Asn Thr Lys Val Met Leu Ser Met Gln Asp Phe Gly					
[3163]		370		375		380
[3164]	Leu Ser Leu Asn Asp Ala Gly Thr Leu Ser Phe Asp Ser Ser Lys Phe					
[3165]		385		390		395
[3166]	Glu Gln Lys Val Lys Glu Asp Pro Asp Ser Thr Glu Ser Phe Phe Ser					
[3167]		405		410		415
[3168]	Asn Ile Thr Lys Tyr Glu Asp Ile Asn His Thr Gly Glu Val Ile Asn					
[3169]		420		425		430
[3170]	Thr Gly Ser Leu Ser Lys Tyr Leu Asn Pro Asn Gly Leu Asp Phe Lys					
[3171]		435		440		445
[3172]	Pro Gly Asp Phe Thr Ile Val Phe Asn Asn Gln Thr Tyr Asp Leu Ser					
[3173]		450		455		460
[3174]	Lys Asn Ser Asp Gly Thr Asn Phe Lys Leu Thr Gly Lys Thr Glu Glu					
[3175]		465		470		475
[3176]	Glu Leu Leu Gln Asn Leu Ala Asn His Ile Asn Ser Lys Gly Ile Glu					
[3177]		485		490		495
[3178]	Gly Leu Lys Val Lys Val Glu Ser Tyr Asn Gln Asn Asn Val Thr Gly					
[3179]		500		505		510
[3180]	Phe Arg Leu Asn Phe Ser Gly Asp Gly Ser Ser Asp Phe Ser Ile Lys					
[3181]		515		520		525
[3182]	Gly Asn Ala Thr Ile Leu Lys Glu Leu Gly Leu Ser Asp Val Asn Ile					
[3183]		530		535		540
[3184]	Thr Ser Lys Pro Ile Glu Gly Lys Gly Ile Phe Ser Lys Leu Lys Ala					
[3185]		545		550		555
						560

[3186]	Thr Leu Gln Glu Met Thr Gly Lys Asp Gly Ser Ile Thr Lys Tyr Asp
[3187]	565 570 575
[3188]	Glu Ser Leu Thr Asn Asp Ile Lys Ser Leu Asn Thr Ser Lys Asp Ser
[3189]	580 585 590
[3190]	Thr Gln Ala Met Ile Asp Thr Arg Tyr Asp Thr Met Ala Asn Gln Trp
[3191]	595 600 605
[3192]	Leu Gln Tyr Glu Ser Ile Leu Asn Lys Leu Asn Gln Gln Leu Asn Thr
[3193]	610 615 620
[3194]	Val Thr Asn Met Ile Asn Ala Ala Asn Asn Ser Asn Asn
[3195]	625 630 635
[3196]	<210> 72
[3197]	<211> 642
[3198]	<212> PRT
[3199]	<213> 人工序列(Artificial Sequence)
[3200]	<220>
[3201]	<223> 合成序列-鞭毛丝加帽
[3202]	蛋白Flid [空肠弯曲杆菌亚种空肠]
[3203]	GenBank: ALF93210.1
[3204]	<400> 72
[3205]	Met Ala Phe Gly Ser Leu Ser Ser Leu Gly Phe Gly Ser Gly Val Leu
[3206]	1 5 10 15
[3207]	Thr Gln Asp Thr Ile Asp Lys Leu Lys Glu Ala Glu Gln Lys Ala Arg
[3208]	20 25 30
[3209]	Ile Asp Pro Tyr Thr Lys Lys Ile Glu Glu Asn Thr Thr Lys Gln Lys
[3210]	35 40 45
[3211]	Asp Leu Thr Glu Ile Lys Thr Lys Leu Leu Ser Phe Gln Thr Ala Val
[3212]	50 55 60
[3213]	Ser Ser Leu Ala Asp Ala Thr Val Phe Ala Lys Arg Lys Val Val Gly
[3214]	65 70 75 80
[3215]	Ser Ile Ser Asp Asn Pro Pro Ala Ser Leu Thr Val Asn Ser Gly Val
[3216]	85 90 95
[3217]	Ala Leu Gln Ser Met Asn Ile Asn Val Thr Gln Leu Ala Gln Lys Asp
[3218]	100 105 110
[3219]	Val Tyr Gln Ser Lys Gly Leu Ala Asn Asp Gly Gly Phe Val Asn Ala
[3220]	115 120 125
[3221]	Gln Leu Asn Gly Thr Ala Asp Leu Thr Phe Phe Ser Asn Gly Lys Glu
[3222]	130 135 140
[3223]	Tyr Thr Val Thr Val Asp Lys Asn Thr Thr Tyr Arg Asp Leu Ala Asp
[3224]	145 150 155 160

[3225]	Lys Ile Asn Glu Ala Ser Gly Gly Glu Ile Val Ala Lys Ile Val Asn
[3226]	165 170 175
[3227]	Thr Gly Glu Lys Gly Thr Pro Tyr Arg Leu Thr Leu Thr Ser Lys Glu
[3228]	180 185 190
[3229]	Thr Gly Glu Asp Ser Ala Ile Ser Phe Tyr Ala Gly Lys Lys Asp Ser
[3230]	195 200 205
[3231]	Asn Gly Lys Tyr Gln Lys Asp Thr Asn Ala Glu Lys Ile Phe Asp Asp
[3232]	210 215 220
[3233]	Leu Gly Trp Gly Leu Asp Ala Ser Ala Ser Ile Asp Pro Ala Lys Asp
[3234]	225 230 235 240
[3235]	Lys Lys Gly Tyr Gly Ile Lys Asp Ala Ser Leu His Ile Gln Thr Ala
[3236]	245 250 255
[3237]	Gln Asn Ala Glu Phe Thr Leu Asp Gly Ile Lys Met Phe Arg Ser Ser
[3238]	260 265 270
[3239]	Asn Thr Val Thr Asp Leu Gly Val Gly Met Thr Leu Thr Leu Asn Lys
[3240]	275 280 285
[3241]	Thr Gly Glu Ile Asn Phe Asp Val Gln Gln Asp Phe Glu Gly Val Thr
[3242]	290 295 300
[3243]	Lys Ala Met Gln Asp Leu Val Asp Ala Tyr Asn Asp Leu Val Thr Asn
[3244]	305 310 315 320
[3245]	Leu Asn Ala Ala Thr Asp Tyr Asn Ser Glu Thr Gly Thr Lys Gly Thr
[3246]	325 330 335
[3247]	Leu Gln Gly Ile Ser Glu Val Asn Ser Ile Arg Ser Ser Ile Leu Ala
[3248]	340 345 350
[3249]	Asp Leu Phe Asp Ser Gln Val Val Asp Gly Thr Thr Glu Asp Ala Asn
[3250]	355 360 365
[3251]	Gly Asn Lys Val Asn Thr Lys Val Met Leu Ser Met Gln Asp Phe Gly
[3252]	370 375 380
[3253]	Leu Ser Leu Asn Asp Ala Gly Thr Leu Asn Phe Asp Ser Ser Lys Phe
[3254]	385 390 395 400
[3255]	Glu Gln Lys Val Lys Glu Asp Pro Asp Ser Ala Glu Ser Phe Phe Ser
[3256]	405 410 415
[3257]	Asn Ile Thr Lys Tyr Glu Asp Ile Asn His Thr Gly Glu Ile Ile Lys
[3258]	420 425 430
[3259]	Thr Gly Asn Leu Ser Lys Tyr Leu Asn Ser Asn Gly Gly Asn Thr Asn
[3260]	435 440 445
[3261]	Gly Leu Asp Phe Lys Pro Gly Asp Phe Thr Ile Val Phe Asn Asn Gln
[3262]	450 455 460
[3263]	Thr Tyr Asp Leu Ser Lys Asn Ser Asp Gly Thr Asn Phe Lys Leu Thr

[3264]	465	470	475	480
[3265]	Gly Lys Thr Glu Glu Glu Leu Leu Gln Asn Leu Ala Asn His Ile Asn			
[3266]		485	490	495
[3267]	Ser Lys Gly Ile Glu Gly Leu Lys Val Lys Val Glu Ser Tyr Asp Gln			
[3268]		500	505	510
[3269]	Asn Asn Val Lys Gly Phe Lys Leu Asn Phe Ser Gly Asp Gly Ser Ser			
[3270]		515	520	525
[3271]	Asp Phe Ser Ile Lys Gly Asp Ala Ser Ile Leu Lys Glu Leu Gly Leu			
[3272]		530	535	540
[3273]	Ser Asp Val Asn Ile Ile Ser Lys Pro Ile Glu Gly Lys Gly Ile Phe			
[3274]	545	550	555	560
[3275]	Ser Lys Leu Lys Ala Thr Leu Gln Glu Met Thr Gly Lys Asp Gly Ser			
[3276]		565	570	575
[3277]	Ile Thr Lys Tyr Asp Glu Ser Leu Thr Asn Asp Ile Lys Ser Leu Asn			
[3278]		580	585	590
[3279]	Thr Ser Lys Asp Ser Thr Gln Ala Met Ile Asp Thr Arg Tyr Asp Thr			
[3280]		595	600	605
[3281]	Met Ala Asn Gln Trp Leu Gln Tyr Glu Ser Ile Leu Asn Lys Leu Asn			
[3282]		610	615	620
[3283]	Gln Gln Leu Asn Thr Val Thr Asn Met Ile Asn Ala Ala Asn Asn Ser			
[3284]	625	630	635	640
[3285]	Asn Asn			
[3286]	<210> 73			
[3287]	<211> 642			
[3288]	<212> PRT			
[3289]	<213> 人工序列(Artificial Sequence)			
[3290]	<220>			
[3291]	<223> 合成序列-鞭毛钩相关			
[3292]	蛋白2 [空肠弯曲杆菌亚种空肠]			
[3293]	GenBank: AJP35034.1			
[3294]	<400> 73			
[3295]	Met Ala Phe Gly Ser Leu Ser Ser Leu Gly Phe Gly Ser Gly Val Leu			
[3296]	1	5	10	15
[3297]	Thr Gln Asp Thr Ile Asp Lys Leu Lys Glu Ala Glu Gln Lys Ala Arg			
[3298]		20	25	30
[3299]	Ile Asp Pro Tyr Thr Lys Lys Ile Glu Glu Asn Thr Thr Lys Gln Lys			
[3300]		35	40	45
[3301]	Asp Leu Thr Glu Ile Lys Thr Lys Leu Leu Ser Phe Gln Thr Ala Val			
[3302]		50	55	60

[3303]	Ser Ser Leu Ala Asp Ala Thr Val Phe Ala Lys Arg Lys Val Val Gly
[3304]	65 70 75 80
[3305]	Ser Ile Ser Asp Asn Pro Pro Ala Ser Leu Thr Val Asn Ser Gly Val
[3306]	85 90 95
[3307]	Ala Leu Gln Ser Met Asn Ile Asn Val Thr Gln Leu Ala Gln Lys Asp
[3308]	100 105 110
[3309]	Val Tyr Gln Ser Gln Gly Leu Ala Asn Asp Gly Gly Phe Val Asn Ala
[3310]	115 120 125
[3311]	Gln Leu Asn Gly Thr Ala Asp Leu Thr Phe Phe Ser Asn Gly Lys Glu
[3312]	130 135 140
[3313]	Tyr Thr Val Thr Val Asp Lys Asn Thr Thr Tyr Arg Asp Leu Ala Asp
[3314]	145 150 155 160
[3315]	Lys Ile Asn Glu Ala Ser Gly Gly Glu Ile Val Ala Lys Ile Val Asn
[3316]	165 170 175
[3317]	Thr Gly Glu Lys Gly Thr Pro Tyr Arg Leu Thr Leu Thr Ser Lys Glu
[3318]	180 185 190
[3319]	Thr Gly Glu Asp Ser Ala Ile Ser Phe Tyr Ala Gly Lys Lys Asp Ala
[3320]	195 200 205
[3321]	Gln Gly Gln Tyr Glu Ser Asp Ser Glu Ala Glu Lys Ile Phe Lys Ser
[3322]	210 215 220
[3323]	Leu Gly Trp Glu Leu Asp Thr Thr Ser Ser Ile Asn Pro Ala Lys Asp
[3324]	225 230 235 240
[3325]	Lys Lys Gly Tyr Gly Ile Lys Asp Ala Ser Leu His Ile Gln Thr Ala
[3326]	245 250 255
[3327]	Gln Asn Ala Glu Phe Thr Leu Asp Gly Ile Lys Met Phe Arg Ser Ser
[3328]	260 265 270
[3329]	Asn Thr Val Thr Asp Leu Gly Val Gly Met Thr Leu Thr Leu Asn Lys
[3330]	275 280 285
[3331]	Thr Gly Glu Ile Asn Phe Asp Val Gln Gln Asp Phe Glu Gly Val Thr
[3332]	290 295 300
[3333]	Lys Ala Met Gln Asp Leu Val Asp Ala Tyr Asn Asp Leu Val Thr Asn
[3334]	305 310 315 320
[3335]	Leu Asn Ala Ala Thr Asp Tyr Asn Ser Glu Thr Gly Thr Lys Gly Thr
[3336]	325 330 335
[3337]	Leu Gln Gly Ile Ser Glu Val Asn Ser Ile Arg Ser Ser Ile Leu Ala
[3338]	340 345 350
[3339]	Asp Leu Phe Asp Ser Gln Val Val Asp Gly Thr Thr Glu Asp Ala Asn
[3340]	355 360 365
[3341]	Gly Asn Lys Val Asn Thr Lys Val Met Leu Ser Met Gln Asp Phe Gly

[3342]	370	375	380
[3343]	Leu Ser Leu Asn Asp Ala Gly Thr Leu Ser Phe Asp Ser Ser Lys Phe		
[3344]	385	390	395 400
[3345]	Glu Gln Lys Val Lys Glu Asp Pro Asp Ser Thr Glu Ser Phe Phe Ser		
[3346]		405 410	415
[3347]	Asn Ile Thr Lys Tyr Glu Asp Ile Asn His Thr Gly Glu Val Ile Lys		
[3348]		420 425	430
[3349]	Thr Gly Ser Leu Ser Lys Tyr Leu Asn Ser Asn Gly Gly Asn Thr Asn		
[3350]		435 440	445
[3351]	Gly Leu Glu Phe Gln Pro Gly Asn Phe Thr Ile Val Phe Asn Asn Gln		
[3352]		450 455	460
[3353]	Thr Tyr Asp Leu Ser Lys Asn Ser Asp Gly Thr Asn Phe Lys Leu Thr		
[3354]		465 470	475 480
[3355]	Gly Lys Thr Glu Glu Glu Leu Leu Gln Asn Leu Ala Asn His Ile Asn		
[3356]		485 490	495
[3357]	Ser Lys Gly Ile Glu Gly Leu Lys Val Lys Val Glu Ser Tyr Asp Gln		
[3358]		500 505	510
[3359]	Asn Gly Val Lys Gly Phe Arg Leu Asn Phe Ser Gly Asp Gly Ser Ser		
[3360]		515 520	525
[3361]	Asp Phe Ser Ile Lys Gly Asp Ala Asn Ile Leu Lys Asp Leu Gly Leu		
[3362]		530 535	540
[3363]	Ser Asp Val Asn Ile Thr Ser Lys Pro Ile Glu Gly Lys Gly Ile Phe		
[3364]		545 550	555 560
[3365]	Ser Lys Leu Lys Ala Thr Leu Gln Glu Met Thr Gly Lys Asp Gly Ser		
[3366]		565 570	575
[3367]	Ile Thr Lys Tyr Asp Glu Ser Leu Thr Asn Asp Ile Lys Ser Leu Asn		
[3368]		580 585	590
[3369]	Thr Ser Lys Asp Ser Thr Gln Ala Met Ile Asp Thr Arg Tyr Asp Thr		
[3370]		595 600	605
[3371]	Met Ala Asn Gln Trp Leu Gln Tyr Glu Ser Ile Leu Asn Lys Leu Asn		
[3372]		610 615	620
[3373]	Gln Gln Leu Asn Thr Val Thr Asn Met Ile Asn Ala Ala Asn Asn Ser		
[3374]		625 630	635 640
[3375]	Asn Asn		
[3376]	<210> 74		
[3377]	<211> 637		
[3378]	<212> PRT		
[3379]	<213> 人工序列(Artificial Sequence)		
[3380]	<220>		

[3381] <223> 合成序列-鞭毛丝加帽
 [3382] 蛋白[空肠弯曲杆菌亚种空肠]
 [3383] GenBank: A0H51565.1
 [3384] <400> 74
 [3385] Met Ala Phe Gly Ser Leu Ser Ser Leu Gly Phe Gly Ser Gly Val Leu
 [3386] 1 5 10 15
 [3387] Thr Gln Asp Thr Ile Asp Lys Leu Lys Glu Ala Glu Gln Lys Ala Arg
 [3388] 20 25 30
 [3389] Ile Asp Pro Tyr Thr Lys Lys Ile Glu Glu Asn Thr Thr Lys Gln Lys
 [3390] 35 40 45
 [3391] Asp Leu Thr Glu Ile Lys Thr Lys Leu Leu Ser Phe Gln Thr Ala Val
 [3392] 50 55 60
 [3393] Ser Ser Leu Ala Asp Ala Thr Val Phe Ala Lys Arg Lys Val Val Gly
 [3394] 65 70 75 80
 [3395] Ser Ile Ser Asp Asn Pro Pro Ala Ser Leu Thr Val Asn Ser Gly Val
 [3396] 85 90 95
 [3397] Ala Leu Gln Ser Met Asn Ile Asn Val Thr Gln Leu Ala Gln Lys Asp
 [3398] 100 105 110
 [3399] Val Tyr Gln Ser Lys Gly Leu Ala Asn Asp Gly Gly Phe Val Asn Ala
 [3400] 115 120 125
 [3401] Gln Leu Asn Gly Thr Ala Asp Leu Thr Phe Phe Ser Asn Gly Lys Glu
 [3402] 130 135 140
 [3403] Tyr Thr Val Thr Val Asp Lys Asn Thr Thr Tyr Arg Asp Leu Ala Asp
 [3404] 145 150 155 160
 [3405] Lys Ile Asn Glu Ala Ser Gly Gly Glu Ile Val Ala Lys Ile Val Asn
 [3406] 165 170 175
 [3407] Thr Gly Glu Lys Gly Thr Pro Tyr Arg Leu Thr Leu Thr Ser Lys Glu
 [3408] 180 185 190
 [3409] Thr Gly Glu Asp Ser Ala Ile Ser Phe Tyr Ala Gly Lys Lys Asp Ser
 [3410] 195 200 205
 [3411] Asn Gly Gln Tyr Gln Ser Asp Ser Glu Ala Glu Asn Ile Phe Ser Asn
 [3412] 210 215 220
 [3413] Leu Gly Trp Glu Leu Asp Lys Thr Ser Ser Ile Asp Pro Ala Lys Asp
 [3414] 225 230 235 240
 [3415] Lys Lys Gly Tyr Gly Ile Lys Asp Ala Ser Leu His Ile Gln Thr Ala
 [3416] 245 250 255
 [3417] Gln Asn Ala Glu Phe Thr Leu Asp Gly Ile Lys Met Phe Arg Ser Ser
 [3418] 260 265 270
 [3419] Asn Thr Val Thr Asp Leu Gly Val Gly Met Thr Leu Thr Leu Asn Lys

[3420]	275	280	285
[3421]	Thr Gly Glu Ile Asn Phe Asp Val Gln Gln Asp Phe Glu Gly Val Thr		
[3422]	290	295	300
[3423]	Lys Ala Met Gln Asp Leu Val Asp Ala Tyr Asn Asp Leu Val Thr Asn		
[3424]	305	310	315
[3425]	Leu Asn Ala Ala Thr Asp Tyr Asn Ser Glu Thr Gly Thr Lys Gly Thr		
[3426]		325	330
[3427]	Leu Gln Gly Ile Ser Glu Val Asn Ser Ile Arg Ser Ser Ile Leu Ala		
[3428]		340	345
[3429]	Asp Leu Phe Asp Ser Gln Val Val Asp Gly Thr Thr Glu Asp Ala Asn		
[3430]		355	360
[3431]	Gly Asn Lys Val Asn Thr Lys Val Met Leu Ser Met Gln Asp Phe Gly		
[3432]		370	375
[3433]	Leu Ser Leu Asn Asp Ala Gly Thr Leu Ser Phe Asp Ser Ser Lys Phe		
[3434]		385	390
[3435]	Glu Gln Lys Val Lys Glu Asp Pro Asp Ser Thr Glu Ser Phe Phe Ser		
[3436]		405	410
[3437]	Asn Ile Thr Lys Tyr Glu Asp Ile Asn His Thr Gly Glu Val Ile Asn		
[3438]		420	425
[3439]	Thr Gly Ser Leu Ser Lys Tyr Leu Asn Pro Asn Gly Leu Asp Phe Lys		
[3440]		435	440
[3441]	Pro Gly Asp Phe Thr Ile Val Phe Asn Asn Gln Thr Tyr Asp Leu Ser		
[3442]		450	455
[3443]	Lys Asn Ser Asp Gly Thr Asn Phe Lys Leu Thr Gly Lys Thr Glu Glu		
[3444]		465	470
[3445]	Glu Leu Leu Gln Asn Leu Ala Asn His Ile Asn Ser Lys Gly Ile Glu		
[3446]		485	490
[3447]	Gly Leu Lys Val Lys Val Glu Ser Tyr Asn Gln Asn Asn Val Thr Gly		
[3448]		500	505
[3449]	Phe Arg Leu Asn Phe Ser Gly Asp Gly Ser Ser Asp Phe Ser Ile Lys		
[3450]		515	520
[3451]	Gly Asn Ala Thr Ile Leu Lys Glu Leu Gly Leu Ser Asp Val Asn Ile		
[3452]		530	535
[3453]	Thr Ser Lys Pro Ile Glu Gly Lys Gly Ile Phe Ser Lys Leu Lys Ala		
[3454]		545	550
[3455]	Thr Leu Gln Glu Met Thr Gly Lys Asp Gly Ser Ile Thr Lys Tyr Asp		
[3456]		565	570
[3457]	Glu Ser Leu Thr Asn Asp Ile Lys Ser Leu Asn Thr Ser Lys Asp Ser		
[3458]		580	585
			590

[3459]	Thr Gln Ala Met Ile Asp Thr Arg Tyr Asp Thr Met Ala Asn Gln Trp
[3460]	595 600 605
[3461]	Leu Gln Tyr Glu Ser Ile Leu Asn Lys Leu Asn Gln Gln Leu Asn Thr
[3462]	610 615 620
[3463]	Val Thr Asn Met Ile Asn Ala Ala Asn Asn Ser Asn Asn
[3464]	625 630 635
[3465]	<210> 75
[3466]	<211> 642
[3467]	<212> PRT
[3468]	<213> 人工序列(Artificial Sequence)
[3469]	<220>
[3470]	<223> 合成序列-鞭毛加帽蛋白
[3471]	[空肠弯曲杆菌亚种空肠CG8421]
[3472]	GenBank: AHY39787.1
[3473]	<400> 75
[3474]	Met Ala Phe Gly Ser Leu Ser Ser Leu Gly Phe Gly Ser Gly Val Leu
[3475]	1 5 10 15
[3476]	Thr Gln Asp Thr Ile Asp Lys Leu Lys Glu Ala Glu Gln Lys Ala Arg
[3477]	20 25 30
[3478]	Ile Asp Pro Tyr Thr Lys Lys Ile Glu Glu Asn Thr Thr Lys Gln Lys
[3479]	35 40 45
[3480]	Asp Leu Thr Glu Ile Lys Thr Lys Leu Leu Ser Phe Gln Thr Ala Val
[3481]	50 55 60
[3482]	Ser Ser Leu Ala Asp Ala Thr Val Phe Ala Lys Arg Lys Val Val Gly
[3483]	65 70 75 80
[3484]	Ser Ile Ser Asp Asn Pro Pro Ala Ser Leu Thr Val Asn Ser Gly Val
[3485]	85 90 95
[3486]	Ala Leu Gln Ser Met Asn Ile Asn Val Thr Gln Leu Ala Gln Lys Asp
[3487]	100 105 110
[3488]	Val Tyr Gln Ser Gln Gly Leu Ala Asn Asp Ser Gly Phe Ile Asn Ala
[3489]	115 120 125
[3490]	Asn Leu Ala Gly Thr Thr Asp Leu Thr Phe Phe Ser Asn Gly Lys Glu
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[3504]	Lys Lys Gly Tyr Gly Ile Lys Asp Ala Ser Leu His Ile Gln Thr Ala
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[3508]	Asn Thr Val Thr Asp Leu Gly Val Gly Met Thr Leu Thr Leu Asn Lys
[3509]	275 280 285
[3510]	Thr Gly Glu Ile Asn Phe Asp Val Gln Gln Asp Phe Glu Gly Val Thr
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[3512]	Lys Ala Met Gln Asp Leu Val Asp Ala Tyr Asn Asp Leu Val Thr Asn
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[3567]	Ile Asp Pro Tyr Thr Lys Lys Ile Glu Glu Asn Thr Thr Lys Gln Lys		
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[3582]			145						150				155				160
[3583]	Lys	Ile	Asn	Glu	Ala	Ser	Gly	Gly	Glu	Ile	Val	Ala	Lys	Ile	Val	Asn	
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[3585]	Thr	Gly	Glu	Lys	Gly	Thr	Pro	Tyr	Arg	Leu	Thr	Leu	Thr	Ser	Lys	Glu	
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[3621]	Thr Tyr Asp Leu Ser Lys Asn Ser Asp Gly Thr Asn Phe Lys Leu Thr
[3622]	465 470 475 480
[3623]	Gly Lys Thr Glu Glu Glu Leu Leu Gln Asn Leu Ala Asn His Ile Asn
[3624]	485 490 495
[3625]	Ser Lys Gly Ile Glu Gly Leu Lys Val Lys Val Glu Ser Tyr Asn Gln
[3626]	500 505 510
[3627]	Asn Asn Val Thr Gly Phe Arg Leu Asn Phe Ser Gly Asp Gly Ser Ser
[3628]	515 520 525
[3629]	Asp Phe Ser Ile Lys Gly Asp Ala Asn Ile Leu Lys Glu Leu Gly Leu
[3630]	530 535 540
[3631]	Ser Asp Val Asn Ile Thr Ser Lys Pro Ile Glu Gly Lys Gly Ile Phe
[3632]	545 550 555 560
[3633]	Ser Lys Leu Lys Ala Thr Leu Gln Glu Met Thr Gly Lys Asp Gly Ser
[3634]	565 570 575
[3635]	Ile Thr Lys Tyr Asp Glu Ser Leu Thr Asn Asp Ile Lys Ser Leu Asn
[3636]	580 585 590
[3637]	Thr Ser Lys Asp Ser Thr Gln Ala Met Ile Asp Thr Arg Tyr Asp Thr
[3638]	595 600 605
[3639]	Met Ala Asn Gln Trp Leu Gln Tyr Glu Ser Ile Leu Asn Lys Leu Asn
[3640]	610 615 620
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[3659]	Asp Leu Thr Glu Ile Lys Thr Lys Leu Leu Ser Phe Gln Thr Ala Val			
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[3661]	Ser Ser Leu Ala Asp Ala Thr Val Phe Ala Lys Arg Lys Val Val Gly			
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[3693]	Leu Asn Ala Ala Thr Asp Tyr Asn Ser Glu Thr Gly Thr Lys Gly Thr
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[3695]	Leu Gln Gly Ile Ser Glu Val Asn Ser Ile Arg Ser Ser Ile Leu Ala
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[3697]	Asp Leu Phe Asp Ser Gln Val Val Asp Gly Thr Thr Glu Asp Ala Asn
[3698]	355 360 365
[3699]	Gly Asn Lys Val Asn Thr Lys Val Met Leu Ser Met Gln Asp Phe Gly
[3700]	370 375 380
[3701]	Leu Ser Leu Asn Asp Ala Gly Thr Leu Ser Phe Asp Ser Ser Lys Phe
[3702]	385 390 395 400
[3703]	Glu Gln Lys Val Lys Glu Asp Pro Asp Ser Thr Glu Ser Phe Phe Ser
[3704]	405 410 415
[3705]	Asn Ile Thr Lys Tyr Glu Asp Ile Asn His Thr Gly Glu Val Ile Lys
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[3707]	Thr Gly Ser Leu Ser Lys Tyr Leu Asn Ser Asn Gly Gly Asn Thr Asn
[3708]	435 440 445
[3709]	Gly Leu Glu Phe Lys Pro Gly Asp Phe Thr Ile Val Phe Asn Asn Gln
[3710]	450 455 460
[3711]	Thr Tyr Asp Leu Ser Lys Asn Ser Asp Gly Thr Asn Phe Lys Leu Thr
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[3713]	Gly Lys Thr Glu Glu Glu Leu Leu Gln Asn Leu Ala Asn His Ile Asn
[3714]	485 490 495
[3715]	Ser Lys Gly Ile Glu Gly Leu Lys Val Lys Val Glu Ser Tyr Asn Gln
[3716]	500 505 510
[3717]	Asn Asn Val Thr Gly Phe Arg Leu Asn Phe Ser Gly Asp Gly Ser Ser
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[3719]	Asp Phe Ser Ile Lys Gly Asp Ala Asn Ile Leu Lys Glu Leu Gly Leu
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[3721]	Ser Asp Val Asn Ile Thr Ser Lys Pro Ile Glu Gly Lys Gly Ile Phe
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[3723]	Ser Lys Leu Lys Ala Thr Leu Gln Glu Met Thr Gly Lys Asp Gly Ser
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[3725]	Ile Thr Lys Tyr Asp Glu Ser Leu Thr Asn Asp Ile Lys Ser Leu Asn
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[3729]	Met Ala Asn Gln Trp Leu Gln Tyr Glu Ser Ile Leu Asn Lys Leu Asn
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[3753]	Ser Ile Ser Asp Asn Pro Pro Ala Ser Leu Thr Val Asn Ser Gly Val			
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[3776]	260 265 270
[3777]	Ser Asn Thr Val Thr Asp Leu Gly Val Gly Met Thr Leu Thr Leu Asn
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[3779]	Lys Thr Gly Glu Ile Asn Phe Asp Val Gln Gln Asp Phe Glu Gly Val
[3780]	290 295 300
[3781]	Thr Lys Ala Met Gln Asp Leu Val Asp Ala Tyr Asn Asp Leu Val Thr
[3782]	305 310 315 320
[3783]	Asn Leu Asn Ala Ala Thr Asp Tyr Asn Ser Glu Thr Gly Thr Lys Gly
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[3785]	Thr Leu Gln Gly Ile Ser Glu Val Asn Ser Ile Arg Ser Ser Ile Leu
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[3787]	Ala Asp Leu Phe Asp Ser Gln Val Val Asp Gly Thr Thr Glu Asp Ala
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[3791]	Gly Leu Ser Leu Asn Asp Ala Gly Thr Leu Ser Phe Asp Ser Ser Lys
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[3807]	Gln Asn Gly Val Lys Gly Phe Lys Leu Asn Phe Ser Gly Asp Gly Ser
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[3809]	Ser Asp Phe Ser Ile Lys Gly Asn Ala Thr Ile Leu Gln Glu Leu Gly

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[3813]	Phe Ser Lys Leu Lys Ala Thr Leu Gln Glu Met Thr Gly Lys Asp Gly		
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[3815]	Ser Ile Thr Lys Tyr Asp Glu Ser Leu Thr Asn Asp Ile Lys Ser Leu		
[3816]	580	585	590
[3817]	Asn Thr Ser Lys Asp Ser Thr Gln Ala Met Ile Asp Thr Arg Tyr Asp		
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[3819]	Thr Met Ala Asn Gln Trp Leu Gln Tyr Glu Ser Ile Leu Asn Lys Leu		
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[3821]	Asn Gln Gln Leu Asn Thr Val Thr Asn Met Ile Asn Ala Ala Asn Asn		
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[3823]	Ser Asn Asn		
[3824]	<210> 79		
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[3841]	Ser Ser Leu Ala Asp Ala Thr Val Phe Ala Lys Arg Lys Val Val Gly		
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[3847]	Val Tyr Gln Ser Lys Gly Leu Ala Asn Asp Ser Gly Phe Ile Asn Ala		
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[3851]	Tyr Thr Val Thr Val Asp Lys Asn Thr Thr Tyr Arg Asp Leu Ala Asp
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[3853]	Lys Ile Asn Glu Ala Ser Gly Gly Glu Ile Val Ala Lys Ile Val Asn
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[3855]	Thr Gly Glu Lys Gly Thr Pro Tyr Arg Leu Thr Leu Thr Ser Lys Glu
[3856]	180 185 190
[3857]	Thr Gly Glu Asp Ser Ala Ile Ser Phe Tyr Ala Gly Lys Lys Asp Ala
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[3859]	Gln Gly Gln Tyr Lys Ser Asp Ser Glu Ala Glu Glu Ile Phe Lys Ser
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[3861]	Leu Gly Trp Glu Leu Asp Thr Ala Ser Ser Ile Asp Pro Ala Lys Asp
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[3863]	Lys Lys Gly Tyr Gly Ile Lys Asp Pro Ser Leu His Ile Gln Thr Ala
[3864]	245 250 255
[3865]	Gln Asn Ala Glu Phe Thr Leu Asp Gly Ile Lys Met Phe Arg Ser Ser
[3866]	260 265 270
[3867]	Asn Thr Val Thr Asp Leu Gly Val Gly Met Thr Leu Thr Leu Asn Lys
[3868]	275 280 285
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[3871]	Lys Ala Met Gln Asp Leu Val Asp Ala Tyr Asn Asp Leu Val Thr Asn
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[3873]	Leu Asn Ala Ala Thr Asp Tyr Asn Ser Glu Thr Gly Thr Lys Gly Thr
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[3881]	Leu Ser Leu Asn Asp Ala Gly Thr Leu Ser Phe Asp Ser Ser Lys Phe
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[3887]	Thr Gly Ser Leu Ser Lys Tyr Leu Thr Asn Gly Leu Glu Phe Lys Pro

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[3894]	485	490	495
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[3925]	Ile Asp Pro Tyr Thr Lys Lys Ile Glu Glu Asn Thr Thr Lys Gln Lys		
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[3929]	Ser Ser Leu Ala Asp Ala Thr Val Phe Ala Lys Arg Lys Val Val Gly
[3930]	65 70 75 80
[3931]	Ser Ile Ser Asp Asn Pro Pro Ala Ser Leu Thr Val Asn Ser Gly Val
[3932]	85 90 95
[3933]	Ala Leu Gln Ser Met Asn Ile Asn Val Thr Gln Leu Ala Gln Lys Asp
[3934]	100 105 110
[3935]	Val Tyr Gln Ser Lys Gly Leu Ala Asn Asp Ser Gly Phe Ile Asn Ala
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[3939]	Tyr Thr Val Thr Val Asp Lys Asn Thr Thr Tyr Arg Asp Leu Ala Asp
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[3945]	Thr Gly Glu Asp Ser Ala Ile Ser Phe Tyr Ala Gly Lys Lys Asp Ser
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[3947]	Asn Gly Gln Tyr Gln Ser Asp Ser Glu Ala Glu Asn Ile Phe Ser Asn
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[3954]	260 265 270
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[3983]	Ser Lys Gly Ile Glu Gly Leu Lys Val Lys Val Glu Ser Tyr Asn Gln		
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[3985]	Asn Asn Val Thr Gly Phe Arg Leu Asn Phe Ser Gly Asp Gly Ser Ser		
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[3987]	Asp Phe Ser Ile Lys Gly Asn Ala Ser Ile Leu Lys Glu Leu Gly Leu		
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[3989]	Ser Asp Val Asn Ile Thr Ser Lys Pro Ile Glu Gly Lys Gly Ile Phe		
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[3991]	Ser Lys Leu Lys Ala Thr Leu Gln Glu Met Thr Gly Lys Asp Gly Ser		
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[3993]	Ile Thr Lys Tyr Asp Glu Ser Leu Thr Asn Asp Ile Lys Ser Leu Asn		
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 [4014] Ile Asn Pro Tyr Thr Lys Lys Ile Glu Glu Asn Thr Thr Lys Gln Lys
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 [4017] 50 55 60
 [4018] Ser Ser Leu Ala Asp Ala Thr Val Phe Ala Lys Arg Lys Val Val Gly
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 [4035] 195 200 205
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 [4039] 225 230 235 240
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 [4042] Gln Asn Ala Glu Phe Thr Leu Asp Gly Ile Lys Met Phe Arg Ser Ser
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[4072]	Gly Leu Lys Val Lys Val Glu Ser Tyr Asn Gln Asn Gly Val Lys Gly
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[4168]	545 550 555 560
[4169]	Ser Lys Leu Lys Ala Thr Leu Gln Glu Met Thr Gly Lys Asp Gly Ser
[4170]	565 570 575
[4171]	Ile Thr Lys Tyr Asp Glu Ser Leu Thr Asn Asp Ile Lys Ser Leu Asn
[4172]	580 585 590
[4173]	Thr Ser Lys Asp Ser Thr Gln Ala Met Ile Asp Thr Arg Tyr Asp Thr
[4174]	595 600 605
[4175]	Met Ala Asn Gln Trp Leu Gln Tyr Glu Ser Ile Leu Asn Lys Leu Asn
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[4266]	610 615 620
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[4277]	Met Ala Phe Gly Ser Leu Ser Ser Leu Gly Phe Gly Ser Gly Val Leu

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[4281]	Ile Asp Pro Tyr Thr Lys Lys Ile Glu Glu Asn Thr Thr Lys Gln Lys			
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[4283]	Asp Leu Thr Glu Ile Lys Thr Lys Leu Leu Ser Phe Gln Thr Ala Val			
[4284]		50	55	60
[4285]	Ser Ser Leu Ala Asp Ala Thr Val Phe Ala Lys Arg Lys Val Val Gly			
[4286]	65	70	75	80
[4287]	Ser Ile Ser Asp Asn Pro Pro Ala Ser Leu Thr Val Asn Ser Gly Val			
[4288]		85	90	95
[4289]	Ala Leu Gln Ser Met Asn Ile Asn Val Thr Gln Leu Ala Gln Lys Asp			
[4290]		100	105	110
[4291]	Val Tyr Gln Ser Lys Gly Leu Ala Asn Asp Gly Gly Phe Val Asn Ala			
[4292]		115	120	125
[4293]	Gln Leu Asn Gly Thr Ala Asp Leu Thr Phe Phe Ser Asn Gly Lys Glu			
[4294]		130	135	140
[4295]	Tyr Thr Val Thr Val Asp Lys Asn Thr Thr Tyr Arg Asp Leu Ala Asp			
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[4297]	Lys Ile Asn Glu Ala Ser Gly Gly Glu Ile Val Ala Lys Ile Val Asn			
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[4299]	Thr Gly Glu Lys Gly Thr Pro Tyr Arg Leu Thr Leu Thr Ser Lys Glu			
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[4301]	Thr Gly Glu Asp Ser Ala Ile Ser Phe Tyr Ala Gly Lys Lys Asp Ser			
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[4303]	Asn Gly Lys Tyr Gln Lys Asp Thr Asn Ala Glu Lys Ile Phe Asp Asp			
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[4305]	Leu Gly Trp Gly Leu Asp Val Ser Ala Ser Ile Asp Pro Ala Lys Asp			
[4306]	225	230	235	240
[4307]	Lys Lys Gly Tyr Gly Ile Lys Asp Thr Ser Leu His Ile Gln Thr Ala			
[4308]		245	250	255
[4309]	Gln Asn Ala Glu Phe Thr Leu Asp Gly Ile Lys Met Phe Arg Ser Ser			
[4310]		260	265	270
[4311]	Asn Thr Val Thr Asp Leu Gly Val Gly Met Thr Leu Thr Leu Asn Lys			
[4312]		275	280	285
[4313]	Thr Gly Glu Ile Asn Phe Asp Val Gln Gln Asp Phe Glu Gly Val Thr			
[4314]		290	295	300
[4315]	Lys Ala Met Gln Asp Leu Val Asp Ala Tyr Asn Asp Leu Val Thr Asn			
[4316]	305	310	315	320

[4317]	Leu Asn Ala Ala Thr Asp Tyr Asn Ser Glu Thr Gly Thr Lys Gly Thr
[4318]	325 330 335
[4319]	Leu Gln Gly Ile Ser Glu Val Asn Ser Ile Arg Ser Ser Ile Leu Ala
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[4321]	Asp Leu Phe Asp Ser Gln Val Val Asp Gly Thr Thr Glu Asp Ala Asn
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[4323]	Gly Asn Lys Val Asn Thr Lys Val Met Leu Ser Met Gln Asp Phe Gly
[4324]	370 375 380
[4325]	Leu Ser Leu Asn Asp Ala Gly Thr Leu Ser Phe Asn Ser Ser Lys Phe
[4326]	385 390 395 400
[4327]	Glu Gln Lys Val Lys Glu Asp Pro Asp Ser Thr Glu Ser Phe Phe Ser
[4328]	405 410 415
[4329]	Asn Ile Thr Lys Tyr Glu Asp Ile Asn His Thr Gly Glu Val Ile Lys
[4330]	420 425 430
[4331]	Thr Gly Ser Leu Ser Lys Tyr Leu Asn Ser Asn Gly Leu Glu Phe Lys
[4332]	435 440 445
[4333]	Pro Gly Asp Phe Thr Ile Val Phe Asn Asn Gln Thr Tyr Asp Leu Ser
[4334]	450 455 460
[4335]	Lys Asn Ser Asp Gly Thr Asn Phe Lys Leu Thr Gly Lys Thr Glu Glu
[4336]	465 470 475 480
[4337]	Glu Leu Leu Gln Asn Leu Ala Asn His Ile Asn Ser Lys Gly Ile Glu
[4338]	485 490 495
[4339]	Gly Leu Lys Val Lys Val Glu Ser Tyr Asn Gln Asn Asn Val Thr Gly
[4340]	500 505 510
[4341]	Phe Arg Leu Asn Phe Ser Gly Asp Gly Ser Ser Asp Phe Ser Ile Lys
[4342]	515 520 525
[4343]	Gly Asn Ala Ser Ile Leu Lys Glu Leu Gly Leu Ser Asp Val Asn Ile
[4344]	530 535 540
[4345]	Thr Ser Lys Pro Ile Glu Gly Lys Gly Ile Phe Ser Lys Leu Lys Ala
[4346]	545 550 555 560
[4347]	Thr Leu Gln Glu Met Thr Gly Lys Asp Gly Ser Ile Thr Lys Tyr Asp
[4348]	565 570 575
[4349]	Glu Ser Leu Thr Asn Asp Ile Lys Ser Leu Asn Thr Ser Lys Asp Ser
[4350]	580 585 590
[4351]	Thr Gln Ala Met Ile Asp Thr Arg Tyr Asp Thr Met Ala Asn Gln Trp
[4352]	595 600 605
[4353]	Leu Gln Tyr Glu Ser Ile Leu Asn Lys Leu Asn Gln Gln Leu Asn Thr
[4354]	610 615 620
[4355]	Val Thr Asn Met Ile Asn Ala Ala Asn Asn Ser Asn Asn

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[4368]		20	25
[4369]	Ile Asp Pro Tyr Thr Lys Lys Ile Glu Glu Asn Thr Thr Lys Gln Lys		
[4370]		35	40
[4371]	Asp Leu Thr Glu Ile Lys Thr Lys Leu Leu Ser Phe Gln Thr Ala Val		
[4372]		50	55
[4373]	Ser Ser Leu Ala Asp Ala Thr Val Phe Ala Lys Arg Lys Val Val Gly		
[4374]		65	70
[4375]	Ser Ile Ser Asp Asn Pro Pro Ala Ser Leu Thr Val Asn Ser Gly Val		
[4376]		85	90
[4377]	Ala Leu Gln Ser Met Asn Ile Asn Val Thr Gln Leu Ala Gln Lys Asp		
[4378]		100	105
[4379]	Val Tyr Gln Ser Lys Gly Leu Ala Asn Asp Gly Gly Phe Val Asn Ala		
[4380]		115	120
[4381]	Gln Leu Asn Gly Thr Ala Asp Leu Thr Phe Phe Ser Asn Gly Lys Glu		
[4382]		130	135
[4383]	Tyr Thr Val Thr Val Asp Lys Asn Thr Thr Tyr Arg Asp Leu Ala Asp		
[4384]		145	150
[4385]	Lys Ile Asn Glu Ala Ser Gly Gly Glu Ile Val Ala Lys Ile Val Asn		
[4386]		165	170
[4387]	Thr Gly Glu Lys Gly Thr Pro Tyr Arg Leu Thr Leu Thr Ser Lys Glu		
[4388]		180	185
[4389]	Thr Gly Glu Asp Ser Ala Ile Ser Phe Tyr Ala Gly Lys Lys Asp Ser		
[4390]		195	200
[4391]	Asn Gly Lys Tyr Thr Ser Asp Ser Glu Ala Glu Thr Ile Phe Lys Asn		
[4392]		210	215
[4393]	Leu Gly Trp Glu Leu Asp Lys Thr Thr Gln Thr Ile Asp Pro Ala Lys		
[4394]		225	230
			235
			240

[4395]	Asp Lys Lys Gly Tyr Gly Ile Lys Asp Ala Ser Leu His Ile Gln Thr
[4396]	245 250 255
[4397]	Ala Gln Asn Ala Glu Phe Thr Leu Asp Gly Ile Lys Met Phe Arg Ser
[4398]	260 265 270
[4399]	Ser Asn Thr Val Thr Asp Leu Gly Val Gly Met Thr Leu Thr Leu Asn
[4400]	275 280 285
[4401]	Lys Thr Gly Glu Ile Asn Phe Asp Val Gln Gln Asp Phe Glu Gly Val
[4402]	290 295 300
[4403]	Thr Lys Ala Met Gln Asp Leu Val Asp Ala Tyr Asn Asp Leu Val Thr
[4404]	305 310 315 320
[4405]	Asn Leu Asn Ala Ala Thr Asp Tyr Asn Ser Glu Thr Gly Thr Lys Gly
[4406]	325 330 335
[4407]	Thr Leu Gln Gly Ile Ser Glu Val Asn Ser Ile Arg Ser Ser Ile Leu
[4408]	340 345 350
[4409]	Ala Asp Leu Phe Asp Ser Gln Val Val Asp Gly Thr Thr Glu Asp Ala
[4410]	355 360 365
[4411]	Asn Gly Asn Lys Val Asn Thr Lys Val Met Leu Ser Met Gln Asp Phe
[4412]	370 375 380
[4413]	Gly Leu Ser Leu Asn Asp Ala Gly Thr Leu Ser Phe Asp Ser Ser Lys
[4414]	385 390 395 400
[4415]	Phe Glu Gln Lys Val Lys Glu Asp Pro Asp Ser Thr Glu Ser Phe Phe
[4416]	405 410 415
[4417]	Ser Asn Ile Thr Lys Tyr Glu Asp Ile Asn His Thr Gly Glu Val Ile
[4418]	420 425 430
[4419]	Lys Thr Gly Ser Leu Ser Lys Tyr Leu Asn Ser Asn Gly Leu Glu Phe
[4420]	435 440 445
[4421]	Lys Pro Gly Asp Phe Thr Ile Val Phe Asn Asn Gln Thr Tyr Asp Leu
[4422]	450 455 460
[4423]	Ser Lys Asn Ser Asp Gly Thr Asn Phe Lys Leu Thr Gly Lys Thr Glu
[4424]	465 470 475 480
[4425]	Glu Glu Leu Leu Gln Asn Leu Ala Asn His Ile Asn Ser Lys Gly Ile
[4426]	485 490 495
[4427]	Glu Gly Leu Lys Val Lys Val Glu Ser Tyr Asn Gln Asn Asn Val Thr
[4428]	500 505 510
[4429]	Gly Phe Arg Leu Asn Phe Ser Gly Asp Gly Ser Ser Asp Phe Ser Ile
[4430]	515 520 525
[4431]	Lys Gly Asn Ala Ser Ile Leu Lys Glu Leu Gly Leu Ser Asp Val Asn
[4432]	530 535 540
[4433]	Ile Thr Ser Lys Pro Ile Glu Gly Lys Gly Ile Phe Ser Lys Leu Lys

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[4435]	Ala Thr Leu Gln Glu Met Thr Gly Lys Asp Gly Ser Ile Thr Lys Tyr			
[4436]		565	570	575
[4437]	Asp Glu Ser Leu Thr Asn Asp Ile Lys Ser Leu Asn Thr Ser Lys Asp			
[4438]		580	585	590
[4439]	Ser Thr Gln Ala Met Ile Asp Thr Arg Tyr Asp Thr Met Ala Asn Gln			
[4440]		595	600	605
[4441]	Trp Leu Gln Tyr Glu Ser Ile Leu Asn Lys Leu Asn Gln Gln Leu Asn			
[4442]		610	615	620
[4443]	Thr Val Thr Asn Met Ile Asn Ala Ala Asn Asn Ser Asn Asn			
[4444]	625	630	635	
[4445]	<210> 86			
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[4448]	<213> 人工序列(Artificial Sequence)			
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[4452]	GenBank: CDL88777.1			
[4453]	<400> 86			
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[4456]	Thr Gln Asp Thr Ile Asp Lys Leu Lys Glu Ala Glu Gln Lys Ala Arg			
[4457]		20	25	30
[4458]	Ile Asp Pro Tyr Thr Lys Lys Ile Glu Glu Asn Thr Thr Lys Gln Lys			
[4459]		35	40	45
[4460]	Asp Leu Thr Glu Ile Lys Thr Lys Leu Leu Ser Phe Gln Thr Ala Val			
[4461]		50	55	60
[4462]	Ser Ser Leu Ala Asp Ala Thr Val Phe Ala Lys Arg Lys Val Val Gly			
[4463]	65	70	75	80
[4464]	Ser Ile Ser Asp Asn Pro Pro Ala Ser Leu Thr Val Asn Ser Gly Val			
[4465]		85	90	95
[4466]	Ala Leu Gln Ser Met Asn Ile Asn Val Thr Gln Leu Ala Gln Lys Asp			
[4467]		100	105	110
[4468]	Val Tyr Gln Ser Lys Gly Leu Ala Asn Asp Ser Gly Phe Ile Asn Ala			
[4469]		115	120	125
[4470]	Asn Leu Thr Gly Thr Thr Asp Leu Thr Phe Phe Ser Asn Gly Lys Glu			
[4471]		130	135	140
[4472]	Tyr Thr Val Thr Val Asp Lys Asn Thr Thr Tyr Arg Asp Leu Ala Asp			

[4473]	145	150	155	160
[4474]	Lys Ile Asn Glu Ala Ser Gly Gly Glu Ile Val Ala Lys Ile Val Asn			
[4475]		165	170	175
[4476]	Thr Gly Glu Lys Gly Thr Pro Tyr Arg Leu Thr Leu Thr Ser Lys Glu			
[4477]		180	185	190
[4478]	Thr Gly Glu Asp Ser Ala Ile Ser Phe Tyr Ala Gly Lys Lys Asp Ser			
[4479]		195	200	205
[4480]	Asn Gly Lys Tyr Thr Ser Asp Ser Glu Ala Glu Thr Ile Phe Lys Asn			
[4481]		210	215	220
[4482]	Leu Gly Trp Glu Leu Asp Thr Thr Ser Ser Ile Asp Pro Ala Lys Asp			
[4483]		225	230	240
[4484]	Lys Lys Gly Tyr Gly Ile Lys Asp Ala Ser Leu His Ile Gln Thr Ala			
[4485]		245	250	255
[4486]	Gln Asn Ala Glu Phe Thr Leu Asp Gly Ile Lys Met Phe Arg Ser Ser			
[4487]		260	265	270
[4488]	Asn Thr Val Thr Asp Leu Gly Val Gly Met Thr Leu Thr Leu Asn Lys			
[4489]		275	280	285
[4490]	Thr Gly Glu Ile Asn Phe Asp Val Gln Gln Asp Phe Glu Gly Val Thr			
[4491]		290	295	300
[4492]	Lys Ala Met Gln Asp Leu Val Asp Ala Tyr Asn Asp Leu Val Thr Asn			
[4493]		305	310	315
[4494]	Leu Asn Ala Ala Thr Asp Tyr Asn Ser Glu Thr Gly Thr Lys Gly Thr			
[4495]		325	330	335
[4496]	Leu Gln Gly Ile Ser Glu Val Asn Ser Ile Arg Ser Ser Ile Leu Ala			
[4497]		340	345	350
[4498]	Asp Leu Phe Asp Ser Gln Val Val Asp Gly Thr Thr Glu Asp Ala Asn			
[4499]		355	360	365
[4500]	Gly Asn Lys Val Asn Thr Lys Val Met Leu Ser Met Gln Asp Phe Gly			
[4501]		370	375	380
[4502]	Leu Ser Leu Asn Asp Ala Gly Thr Leu Ser Phe Asp Ser Ser Lys Phe			
[4503]		385	390	395
[4504]	Glu Gln Lys Val Lys Glu Asp Pro Asp Ser Thr Glu Ser Phe Phe Ser			
[4505]		405	410	415
[4506]	Asn Ile Thr Lys Tyr Glu Asp Ile Asn His Thr Gly Glu Val Ile Lys			
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[4508]	Gln Gly Ser Leu Asn Gln Tyr Leu Asp Ser Ser Gly Thr Gly Asn Lys			
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[4510]	Gly Leu Asp Phe Lys Pro Gly Asp Phe Thr Ile Val Phe Asn Asn Gln			
[4511]		450	455	460

[4512]	Thr Tyr Asp Leu Ser Lys Asn Ser Asp Gly Thr Asn Phe Lys Leu Thr
[4513]	465 470 475 480
[4514]	Gly Lys Thr Glu Glu Glu Leu Leu Gln Asn Leu Ala Asn His Ile Asn
[4515]	485 490 495
[4516]	Ser Lys Gly Ile Glu Gly Leu Lys Val Lys Val Glu Ser Tyr Asp Gln
[4517]	500 505 510
[4518]	Asn Gly Val Lys Gly Phe Lys Leu Asn Phe Ser Gly Asp Gly Ser Ser
[4519]	515 520 525
[4520]	Asp Phe Ser Ile Lys Gly Asn Ala Thr Ile Leu Lys Glu Leu Gly Leu
[4521]	530 535 540
[4522]	Ser Asp Val Asn Ile Thr Ser Lys Pro Ile Glu Gly Lys Gly Ile Phe
[4523]	545 550 555 560
[4524]	Ser Lys Leu Lys Ala Thr Leu Gln Glu Met Thr Gly Lys Asp Gly Ser
[4525]	565 570 575
[4526]	Ile Thr Lys Tyr Asp Glu Ser Leu Thr Asn Asp Ile Lys Ser Leu Asn
[4527]	580 585 590
[4528]	Thr Ser Lys Asp Ser Thr Gln Ala Met Ile Asp Thr Arg Tyr Asp Thr
[4529]	595 600 605
[4530]	Met Ala Asn Gln Trp Leu Gln Tyr Glu Ser Ile Leu Asn Lys Leu Asn
[4531]	610 615 620
[4532]	Gln Gln Leu Asn Thr Val Thr Asn Met Ile Asn Ala Ala Asn Asn Ser
[4533]	625 630 635 640
[4534]	Asn Asn
[4535]	<210> 87
[4536]	<211> 637
[4537]	<212> PRT
[4538]	<213> 人工序列(Artificial Sequence)
[4539]	<220>
[4540]	<223> 合成序列-鞭毛钩相关
[4541]	蛋白2 (fliD),假定的[大肠弯曲杆菌
[4542]	RM2228] GenBank: EAL57379.1
[4543]	<400> 87
[4544]	Met Ala Phe Gly Ser Leu Ser Ser Leu Gly Phe Gly Ser Gly Val Leu
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[4547]	20 25 30
[4548]	Ile Asp Pro Tyr Thr Lys Lys Ile Glu Glu Asn Thr Thr Lys Gln Lys
[4549]	35 40 45
[4550]	Asp Leu Thr Glu Ile Lys Thr Lys Leu Leu Ser Phe Gln Thr Ala Val

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[4552]	Ser Ser Leu Ala Asp Ala Thr Val Phe Ala Lys Arg Lys Val Val Gly		
[4553]	65	70	75
[4554]	Ser Ile Ser Asp Asn Pro Pro Ala Ser Leu Thr Val Asn Ser Gly Val		
[4555]	85	90	95
[4556]	Ala Leu Gln Ser Met Asn Ile Asn Val Thr Gln Leu Ala Gln Lys Asp		
[4557]	100	105	110
[4558]	Val Tyr Gln Ser Lys Gly Leu Ala Asn Asp Gly Gly Phe Val Asn Ala		
[4559]	115	120	125
[4560]	Gln Leu Asn Gly Thr Ala Asp Leu Thr Phe Phe Ser Asn Gly Lys Glu		
[4561]	130	135	140
[4562]	Tyr Thr Val Thr Val Asp Lys Asn Thr Thr Tyr Arg Asp Leu Ala Asp		
[4563]	145	150	155
[4564]	Lys Ile Asn Glu Ala Ser Gly Gly Glu Ile Val Ala Lys Ile Val Asn		
[4565]	165	170	175
[4566]	Thr Gly Glu Lys Gly Thr Pro Tyr Arg Leu Thr Leu Thr Ser Lys Glu		
[4567]	180	185	190
[4568]	Thr Gly Glu Asp Ser Ala Ile Ser Phe Tyr Ala Gly Lys Lys Asp Ser		
[4569]	195	200	205
[4570]	Asn Gly Lys Tyr Gln Lys Asp Thr Asn Ala Glu Lys Ile Phe Asp Asp		
[4571]	210	215	220
[4572]	Leu Gly Trp Gly Leu Asp Val Ser Ala Ser Ile Asp Pro Ala Lys Asp		
[4573]	225	230	235
[4574]	Lys Lys Gly Tyr Gly Ile Lys Asp Thr Ser Leu His Ile Gln Thr Ala		
[4575]	245	250	255
[4576]	Gln Asn Ala Glu Phe Thr Leu Asp Gly Ile Lys Met Phe Arg Ser Ser		
[4577]	260	265	270
[4578]	Asn Thr Val Thr Asp Leu Gly Val Gly Met Thr Leu Thr Leu Asn Lys		
[4579]	275	280	285
[4580]	Thr Gly Glu Ile Asn Phe Asp Val Gln Gln Asp Phe Glu Gly Val Thr		
[4581]	290	295	300
[4582]	Lys Ala Met Gln Asp Leu Val Asp Ala Tyr Asn Asp Leu Val Thr Asn		
[4583]	305	310	315
[4584]	Leu Asn Ala Ala Thr Asp Tyr Asn Ser Glu Thr Gly Thr Lys Gly Thr		
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[4586]	Leu Gln Gly Ile Ser Glu Val Asn Ser Ile Arg Ser Ser Ile Leu Ala		
[4587]	340	345	350
[4588]	Asp Leu Phe Asp Ser Gln Val Val Asp Gly Thr Thr Glu Asp Ala Asn		
[4589]	355	360	365

[4590]	Gly Asn Lys Val Asn Thr Lys Val Met Leu Ser Met Gln Asp Phe Gly
[4591]	370 375 380
[4592]	Leu Ser Leu Asn Asp Ala Gly Thr Leu Ser Phe Asn Ser Ser Lys Phe
[4593]	385 390 395 400
[4594]	Glu Gln Lys Val Lys Glu Asp Pro Asp Ser Thr Glu Ser Phe Phe Ser
[4595]	405 410 415
[4596]	Asn Ile Thr Lys Tyr Glu Asp Ile Asn His Thr Gly Glu Val Ile Lys
[4597]	420 425 430
[4598]	Thr Gly Ser Leu Ser Lys Tyr Leu Asn Ser Asn Gly Leu Glu Phe Lys
[4599]	435 440 445
[4600]	Pro Gly Asp Phe Thr Ile Val Phe Asn Asn Gln Thr Tyr Asp Leu Ser
[4601]	450 455 460
[4602]	Lys Asn Ser Asp Gly Thr Asn Phe Lys Leu Thr Gly Lys Thr Glu Glu
[4603]	465 470 475 480
[4604]	Glu Leu Leu Gln Asn Leu Ala Asn His Ile Asn Ser Lys Gly Ile Glu
[4605]	485 490 495
[4606]	Gly Leu Lys Val Lys Val Glu Ser Tyr Asn Gln Asn Asn Val Thr Gly
[4607]	500 505 510
[4608]	Phe Arg Leu Asn Phe Ser Gly Asp Gly Ser Ser Asp Phe Ser Ile Lys
[4609]	515 520 525
[4610]	Gly Asn Ala Ser Ile Leu Lys Glu Leu Gly Leu Ser Asp Val Asn Ile
[4611]	530 535 540
[4612]	Thr Ser Lys Pro Ile Glu Gly Lys Gly Ile Phe Ser Lys Leu Lys Ala
[4613]	545 550 555 560
[4614]	Thr Leu Gln Glu Met Thr Gly Lys Asp Gly Ser Ile Thr Lys Tyr Asp
[4615]	565 570 575
[4616]	Glu Ser Leu Thr Asn Asp Ile Lys Ser Leu Asn Thr Ser Lys Asp Ser
[4617]	580 585 590
[4618]	Thr Gln Ala Met Ile Asp Thr Arg Tyr Asp Thr Met Ala Asn Gln Trp
[4619]	595 600 605
[4620]	Leu Gln Tyr Glu Ser Ile Leu Asn Lys Leu Asn Gln Gln Leu Asn Thr
[4621]	610 615 620
[4622]	Val Thr Asn Met Ile Asn Ala Ala Asn Asn Ser Asn Asn
[4623]	625 630 635
[4624]	<210> 88
[4625]	<211> 637
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[4628]	<220>

[4629] <223> 合成序列-鞭毛丝加帽
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 [4639] Asp Leu Thr Glu Ile Lys Thr Lys Leu Leu Ser Phe Gln Thr Ala Val
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 [4641] Ser Ser Leu Ala Asp Ala Thr Val Phe Ala Lys Arg Lys Val Val Gly
 [4642] 65 70 75 80
 [4643] Ser Ile Ser Asp Asn Pro Pro Ala Ser Leu Thr Val Asn Ser Gly Val
 [4644] 85 90 95
 [4645] Ala Leu Gln Ser Met Asn Ile Asn Val Thr Gln Leu Ala Gln Lys Asp
 [4646] 100 105 110
 [4647] Val Tyr Gln Ser Lys Gly Leu Ala Asn Asp Gly Gly Phe Val Asn Ala
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 [4649] Gln Leu Asn Gly Thr Ala Asp Leu Thr Phe Phe Ser Asn Gly Lys Glu
 [4650] 130 135 140
 [4651] Tyr Thr Val Thr Val Asp Lys Asn Thr Thr Tyr Arg Asp Leu Ala Asp
 [4652] 145 150 155 160
 [4653] Lys Ile Asn Glu Ala Ser Gly Gly Glu Ile Val Ala Lys Ile Val Asn
 [4654] 165 170 175
 [4655] Thr Gly Glu Lys Gly Thr Pro Tyr Arg Leu Thr Leu Thr Ser Lys Glu
 [4656] 180 185 190
 [4657] Thr Gly Glu Asp Ser Ala Ile Ser Phe Tyr Ala Gly Lys Lys Asp Ser
 [4658] 195 200 205
 [4659] Asn Gly Lys Tyr Gln Lys Asp Thr Asn Ala Glu Lys Ile Phe Asp Asp
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 [4661] Leu Gly Trp Gly Leu Asp Val Ser Ala Ser Ile Asp Pro Ala Lys Asp
 [4662] 225 230 235 240
 [4663] Lys Lys Gly Tyr Gly Ile Lys Asp Thr Ser Leu His Ile Gln Thr Ala
 [4664] 245 250 255
 [4665] Gln Asn Ala Glu Phe Thr Leu Asp Gly Ile Lys Met Phe Arg Ser Ser
 [4666] 260 265 270
 [4667] Asn Thr Val Thr Asp Leu Gly Val Gly Met Thr Leu Thr Leu Asn Lys

[4668]	275	280	285
[4669]	Thr Gly Glu Ile Asn Phe Asp Val Gln Gln Asp Phe Glu Gly Val Thr		
[4670]	290	295	300
[4671]	Lys Ala Met Gln Asp Leu Val Asp Ala Tyr Asn Asp Leu Val Thr Asn		
[4672]	305	310	315
[4673]	Leu Asn Ala Ala Thr Asp Tyr Asn Ser Glu Thr Gly Thr Lys Gly Thr		
[4674]	325	330	335
[4675]	Leu Gln Gly Ile Ser Glu Val Asn Ser Ile Arg Ser Ser Ile Leu Ala		
[4676]	340	345	350
[4677]	Asp Leu Phe Asp Ser Gln Val Val Asp Gly Thr Thr Glu Asp Ala Asn		
[4678]	355	360	365
[4679]	Gly Asn Lys Val Asn Thr Lys Val Met Leu Ser Met Gln Asp Phe Gly		
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[4681]	Leu Ser Leu Asn Asp Ala Gly Thr Leu Ser Phe Asp Ser Ser Lys Phe		
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[4683]	Glu Gln Lys Val Lys Glu Asp Pro Asp Ser Thr Glu Ser Phe Phe Ser		
[4684]	405	410	415
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[5096]	Asn Leu Thr Gly Thr Thr Asp Leu Thr Phe Phe Ser Asn Gly Lys Glu

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[5103]	180	185	190
[5104]	Thr Gly Glu Asp Ser Ala Ile Ser Phe Tyr Ala Gly Lys Lys Asp Ser		
[5105]	195	200	205
[5106]	Asn Gly Gln Tyr Gln Ser Asp Ser Glu Ala Glu Asn Ile Phe Ser Asn		
[5107]	210	215	220
[5108]	Leu Gly Trp Glu Leu Asp Lys Thr Ser Ser Ile Asp Pro Ala Lys Asp		
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[5112]	Gln Asn Ala Glu Phe Thr Leu Asp Gly Ile Lys Met Phe Arg Ser Ser		
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[5114]	Asn Thr Val Thr Asp Leu Gly Val Gly Met Thr Leu Thr Leu Asn Lys		
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[5141]	485 490 495
[5142]	Ser Lys Gly Ile Glu Gly Leu Lys Val Lys Val Glu Ser Tyr Asn Gln
[5143]	500 505 510
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[5145]	515 520 525
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[5148]	Ser Asp Val Asn Ile Thr Ser Lys Pro Ile Glu Gly Lys Gly Ile Phe
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[5174]	Ile Asp Pro Tyr Thr Lys Lys Ile Glu Glu Asn Thr Thr Lys Gln Lys

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[5178]	Ser Ser Leu Ala Asp Ala Thr Val Phe Ala Lys Arg Lys Val Val Gly		
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[5180]	Ser Ile Ser Asp Asn Pro Pro Ala Ser Leu Thr Val Asn Ser Gly Val		
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[5215]	355 360 365
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[5294]	Asn Thr Val Thr Asp Leu Gly Val Gly Met Thr Leu Thr Leu Asn Lys
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[5337]		610						615						620			
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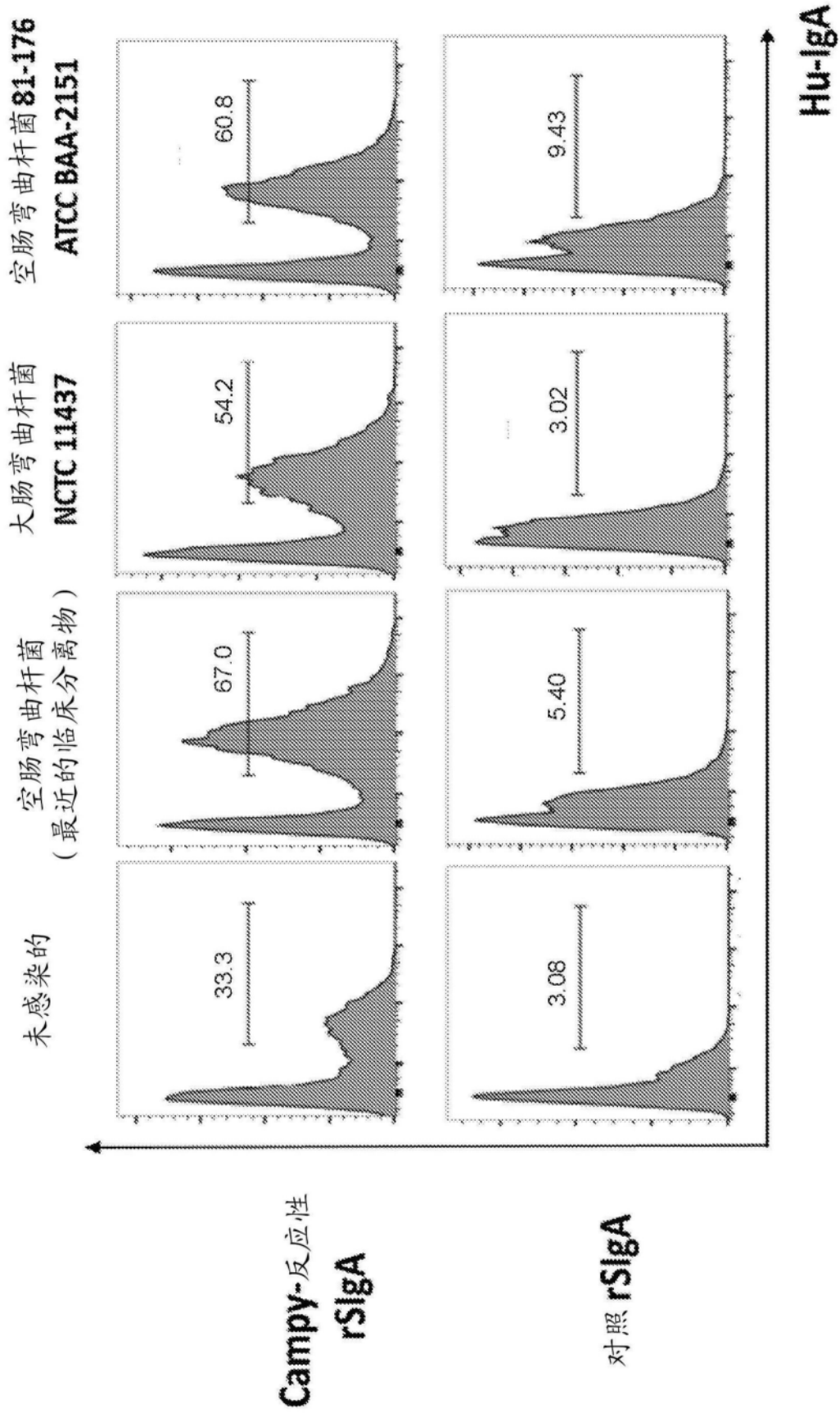


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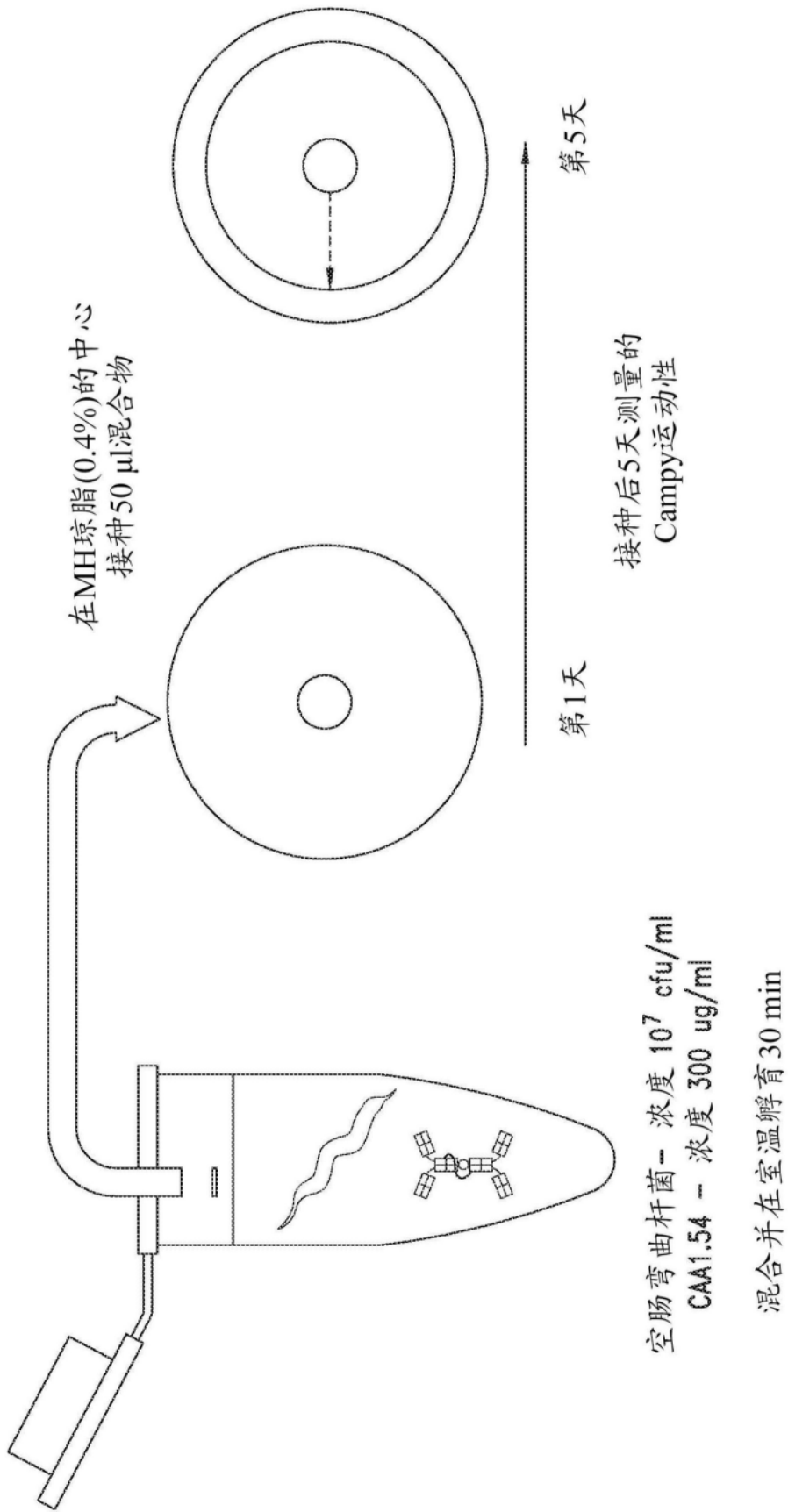


图2

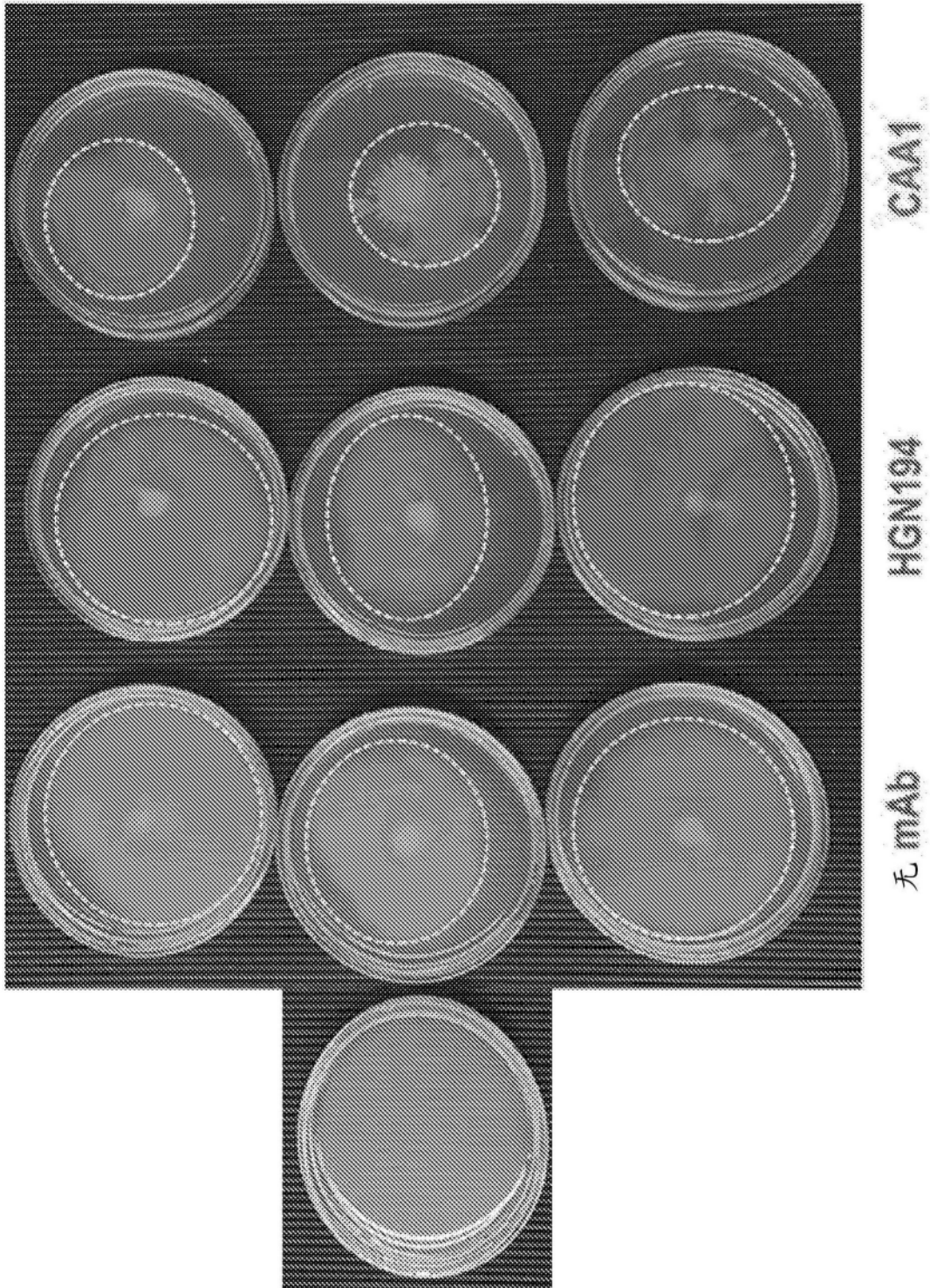


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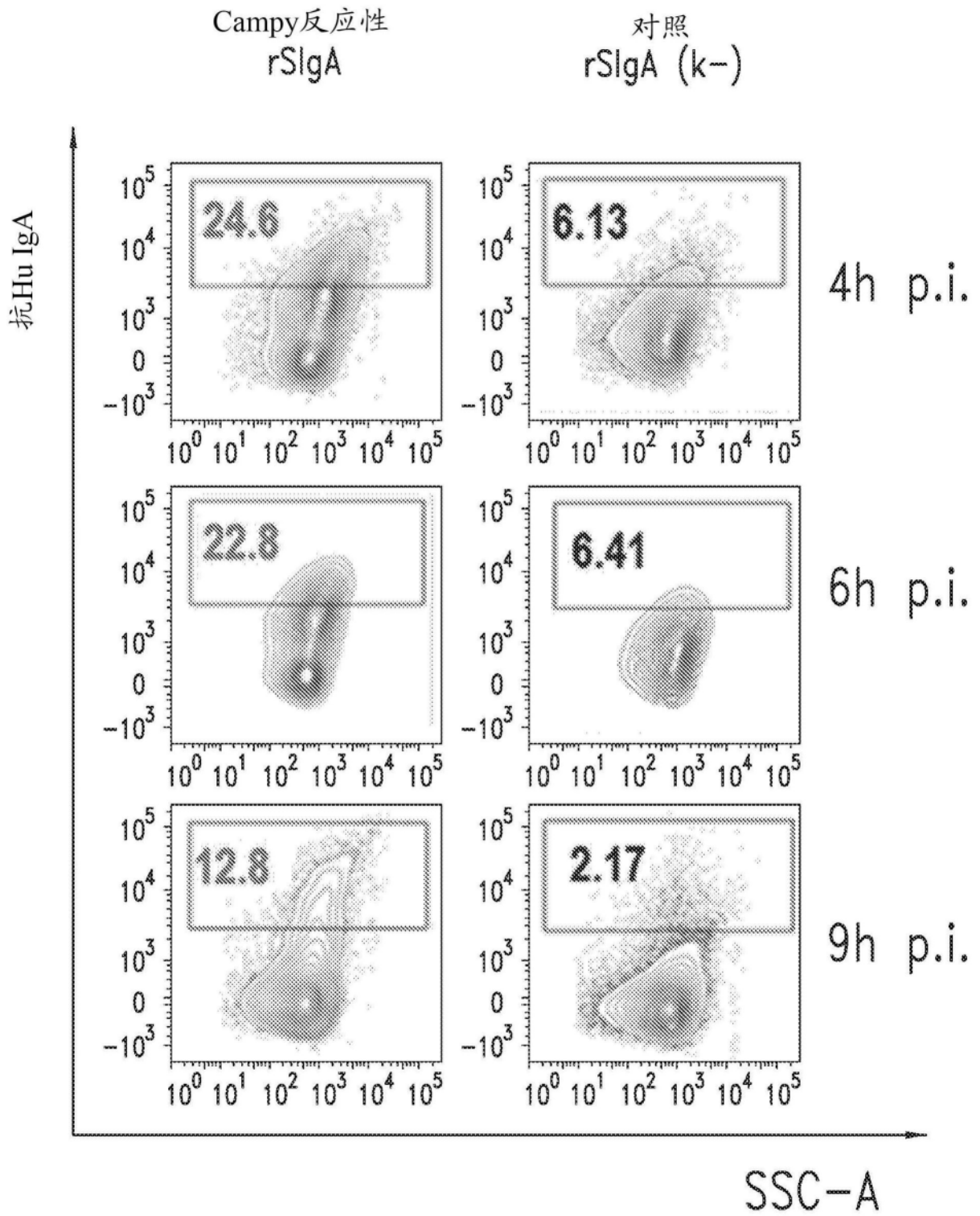


图4A

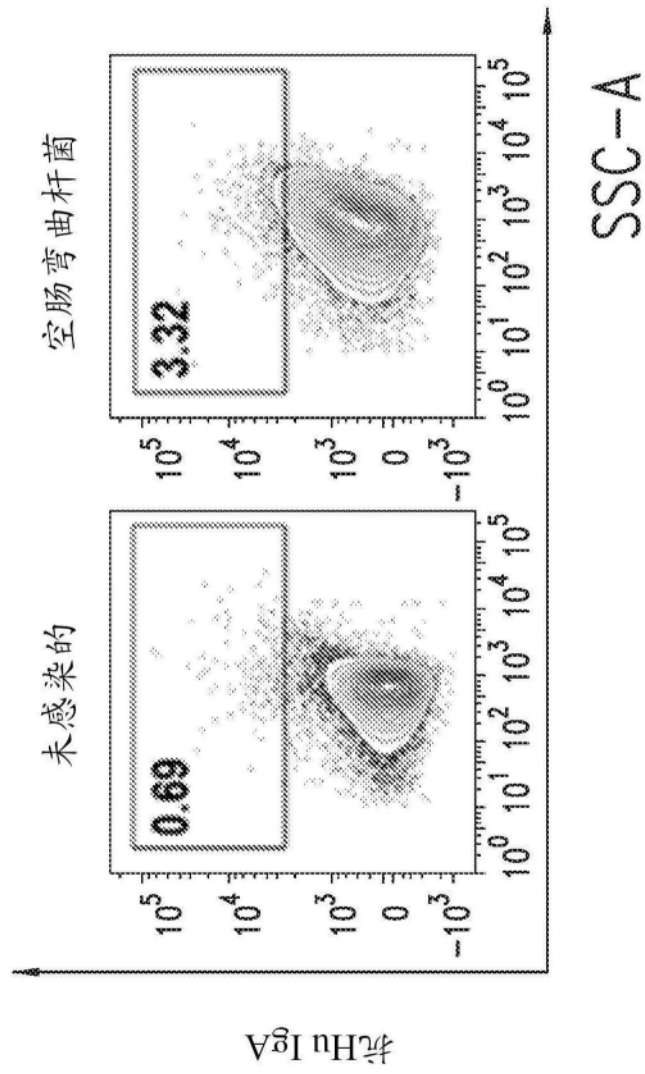


图4B

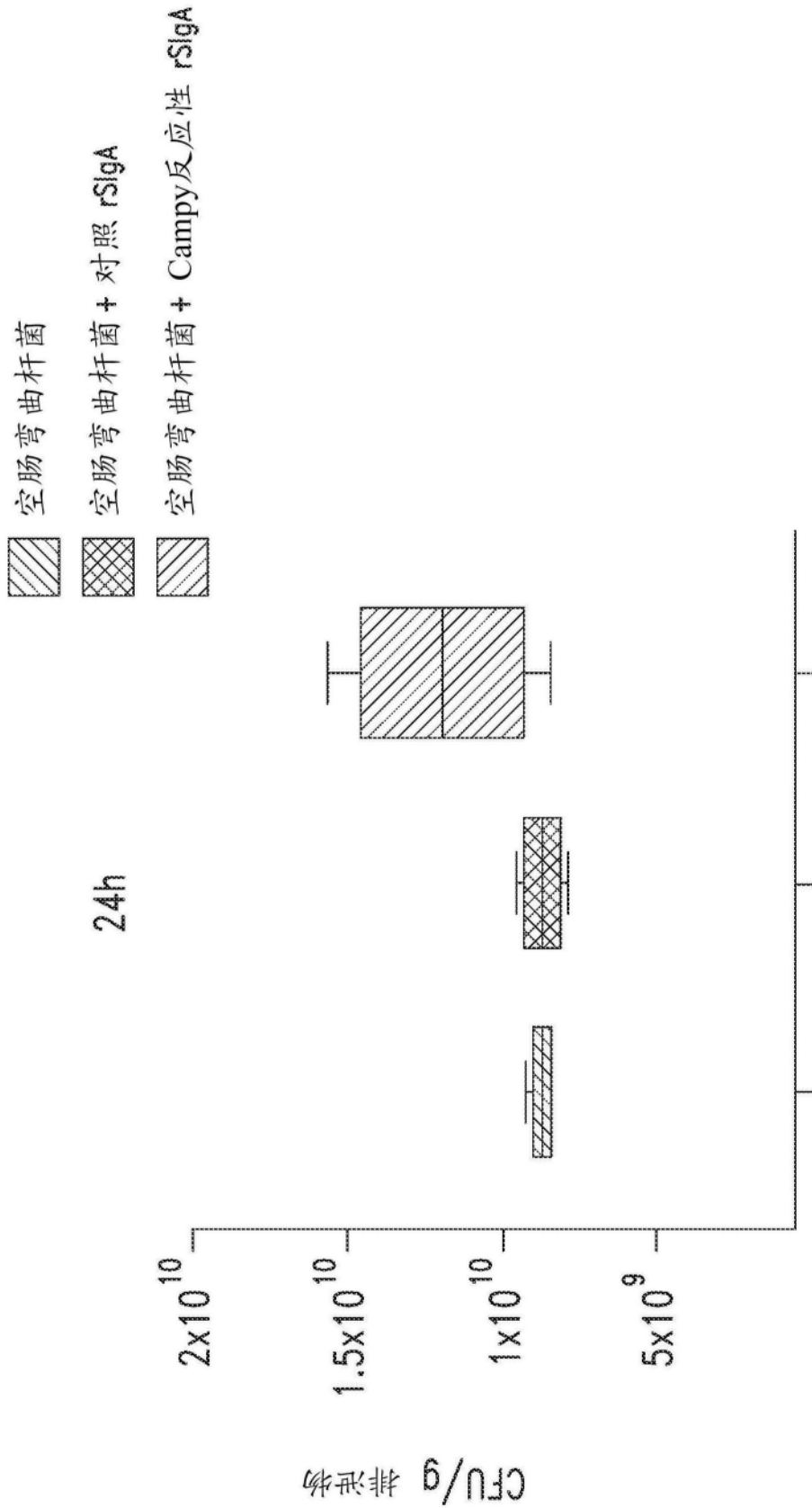


图5A

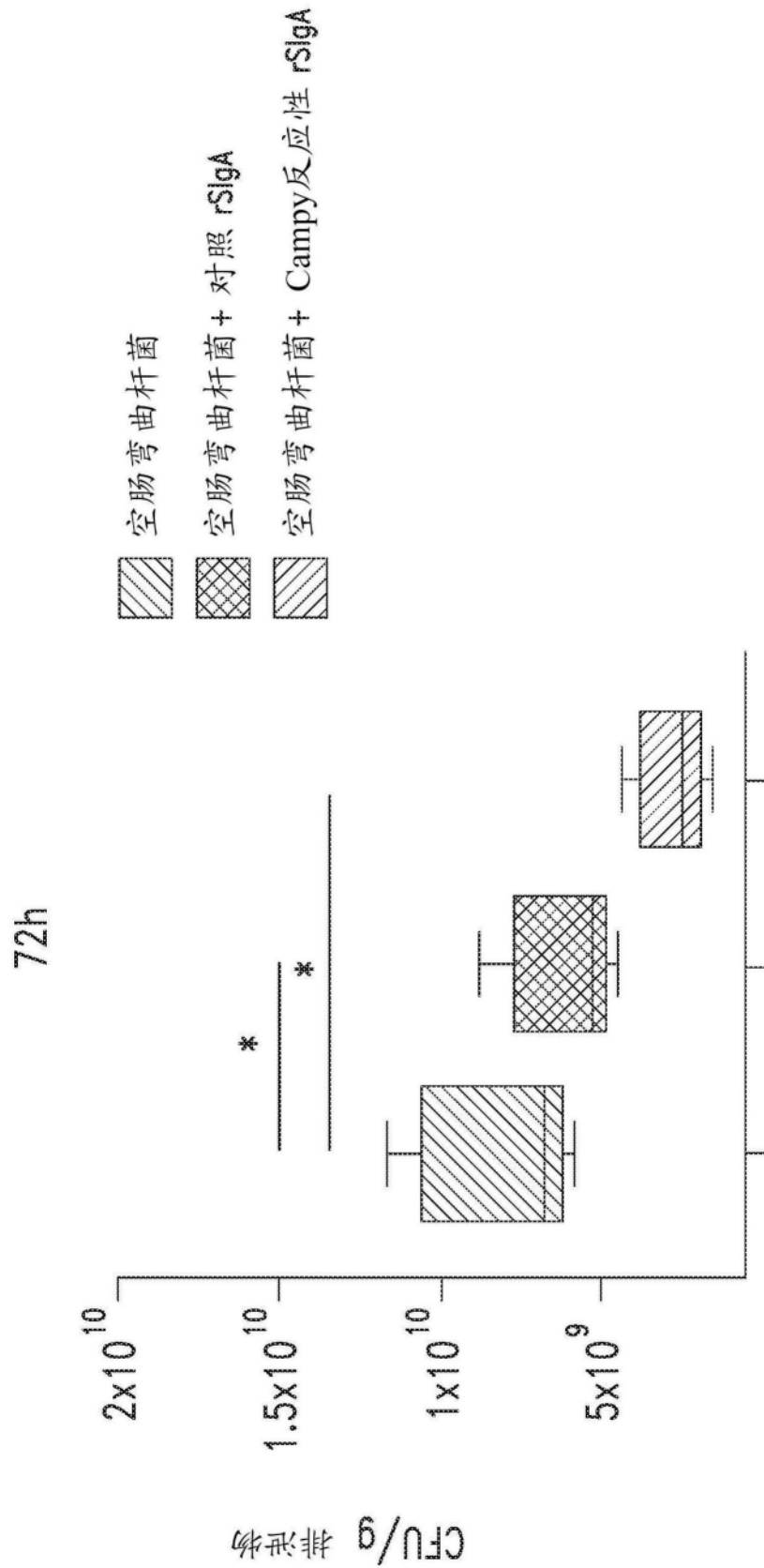


图5B

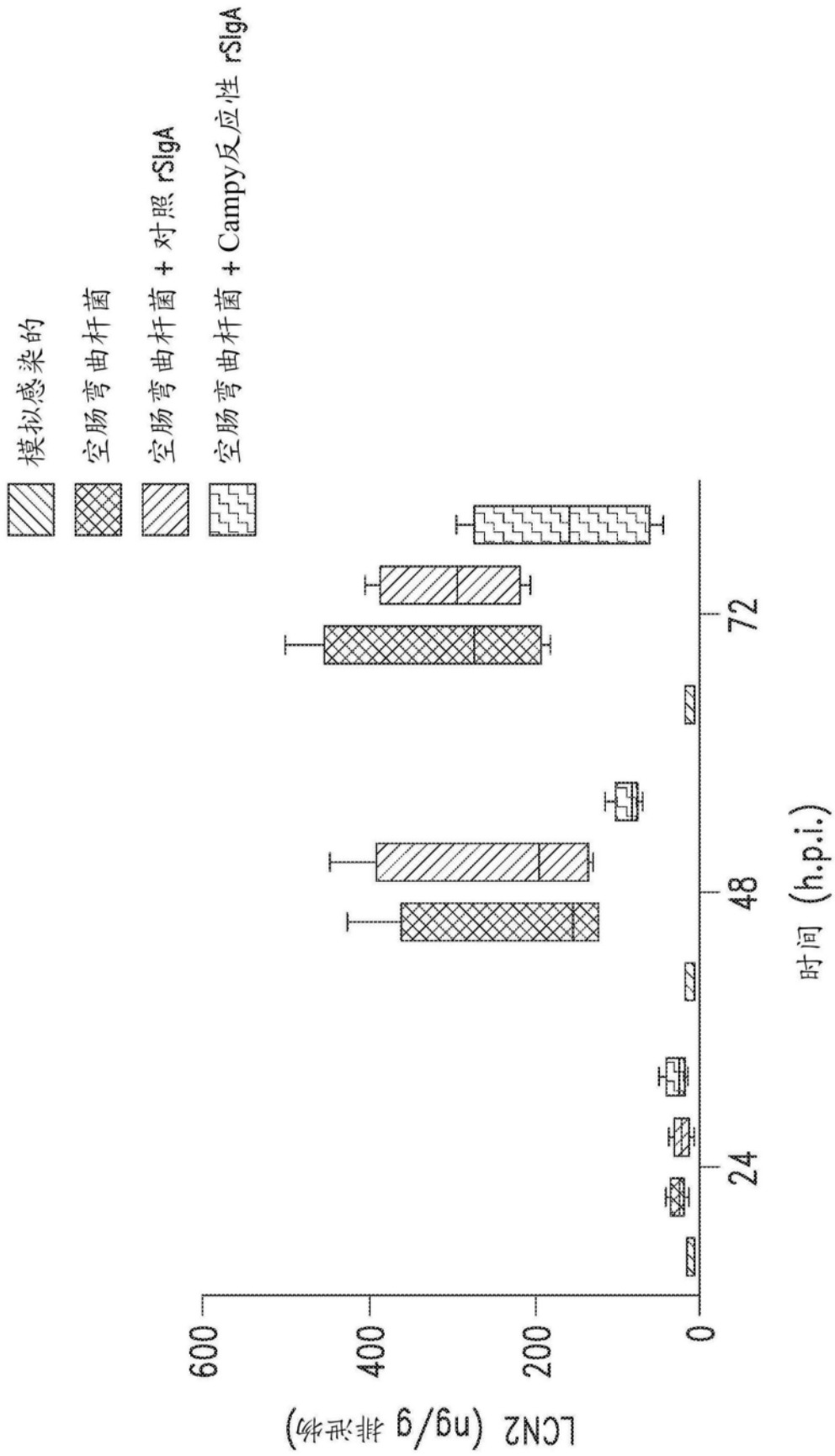


图6

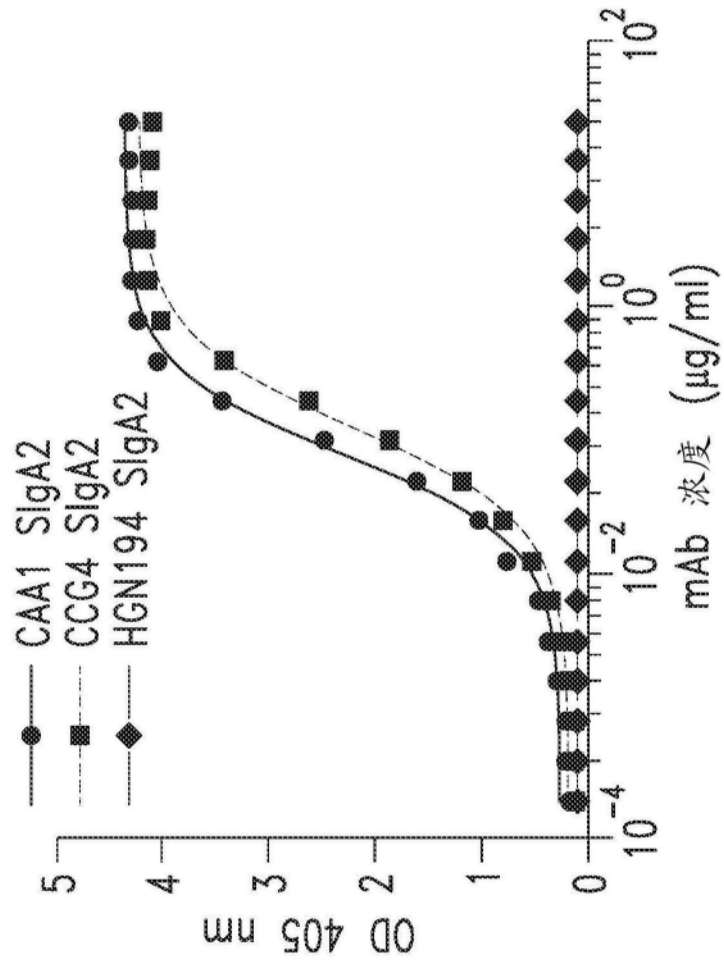


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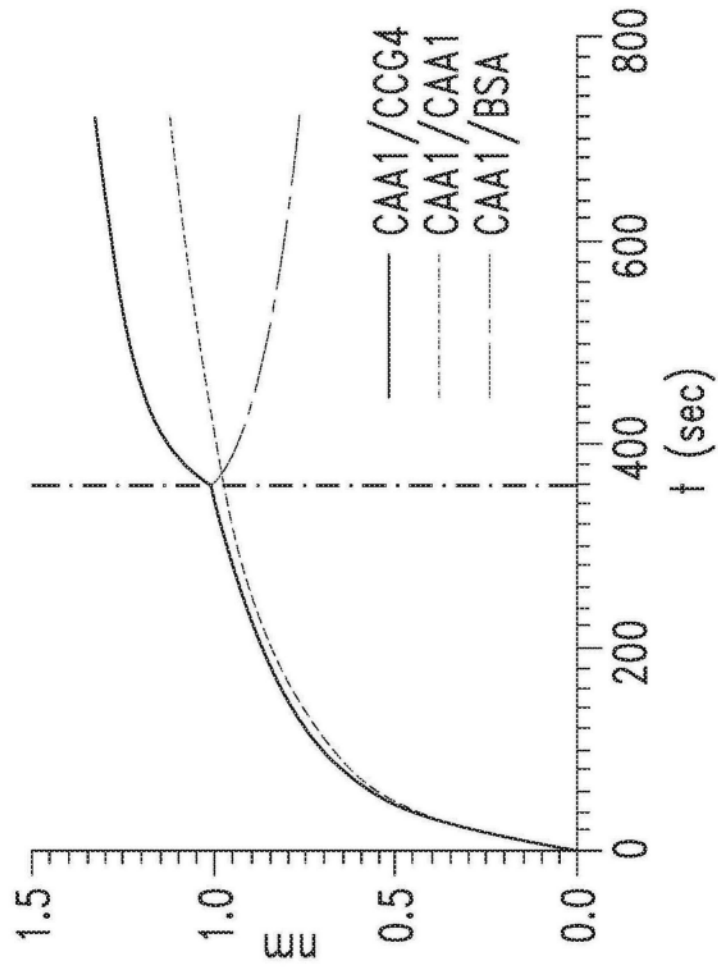


图7B

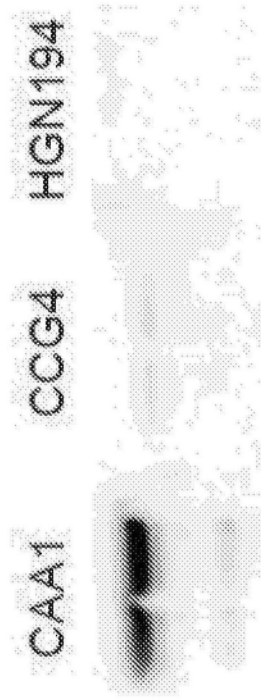


图7C

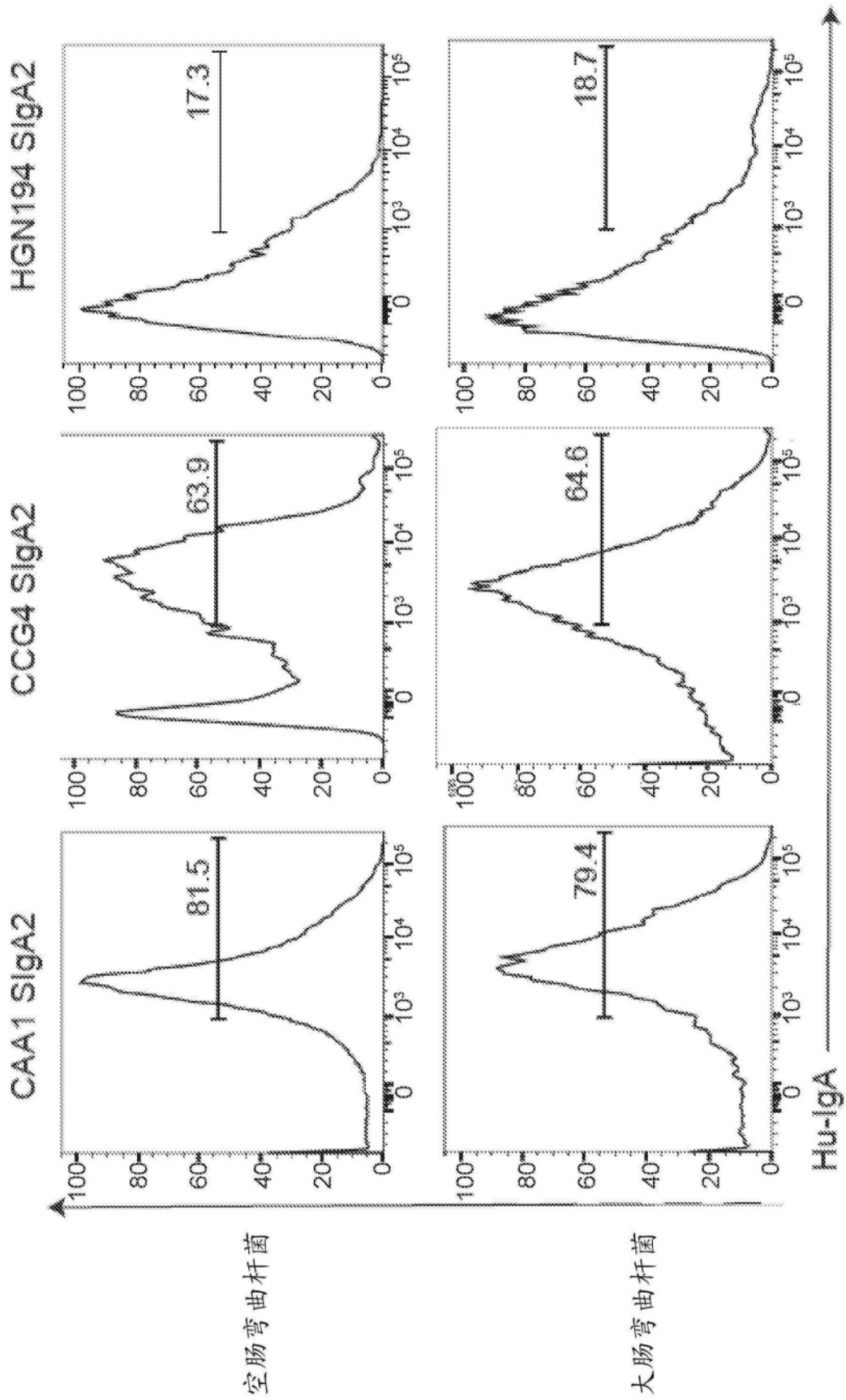


图7D

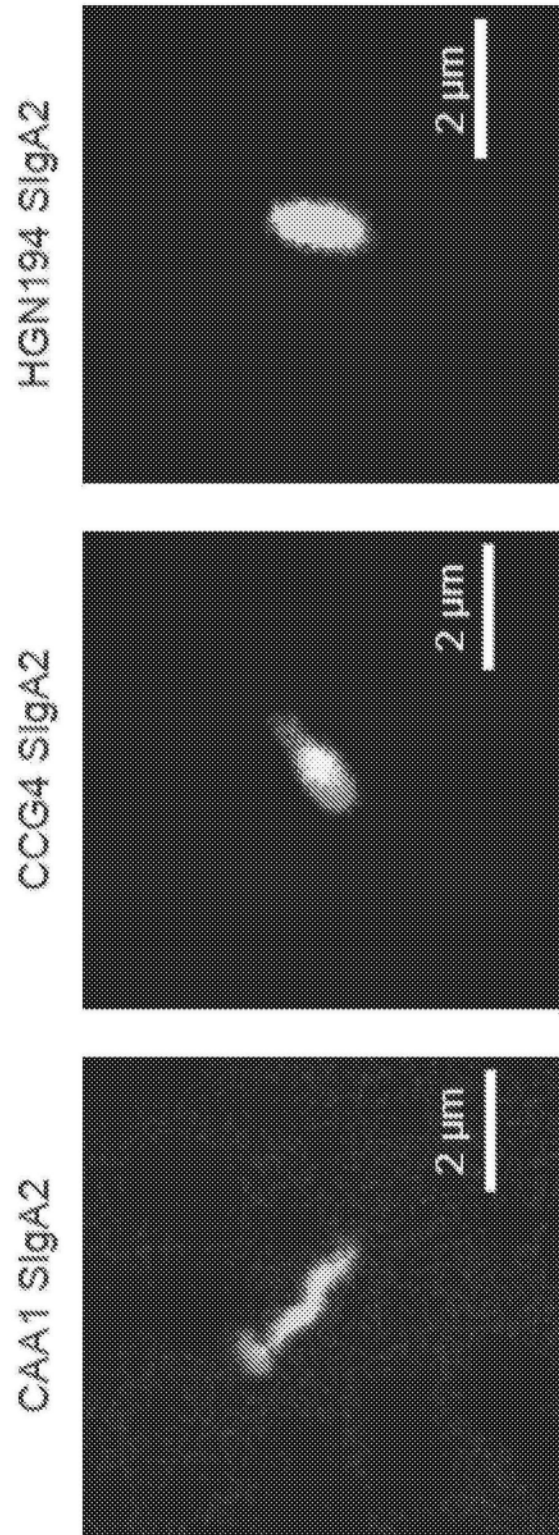


图7E

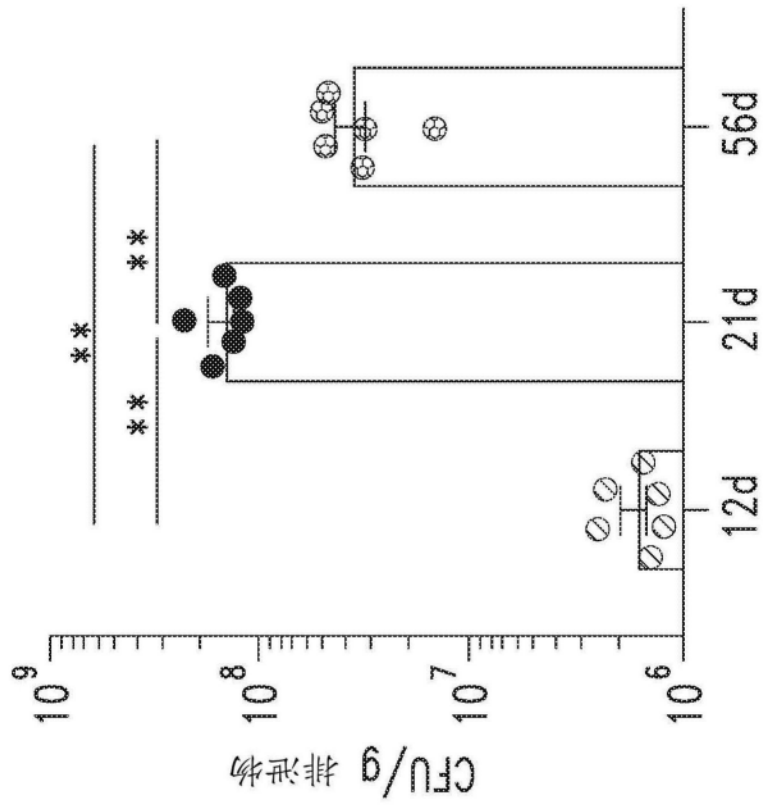


图8A

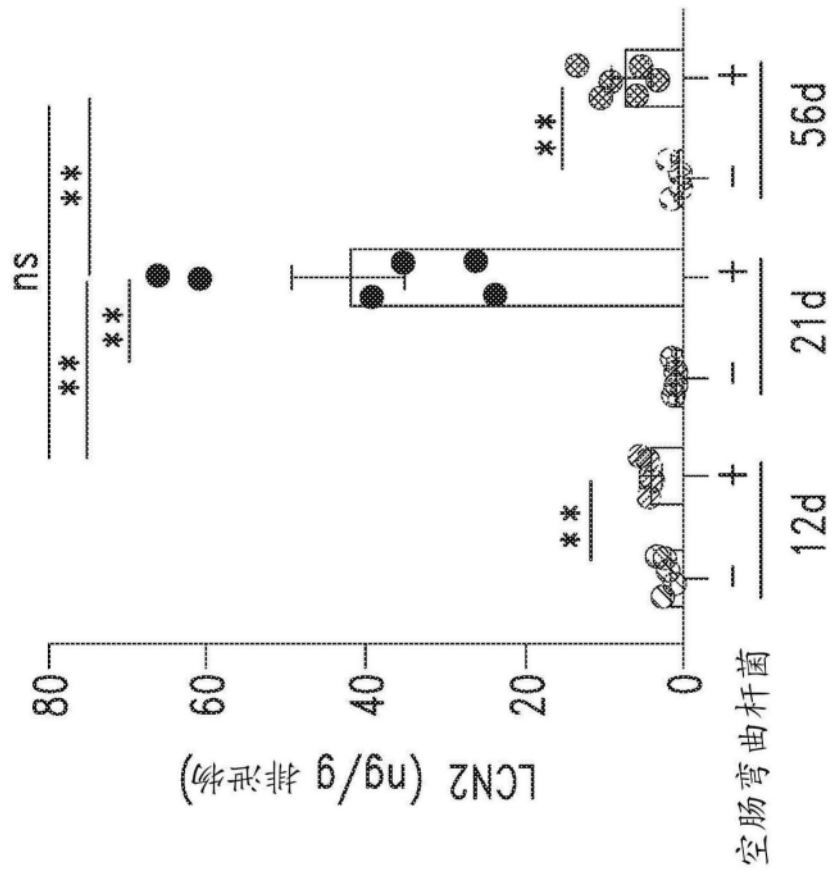


图8B

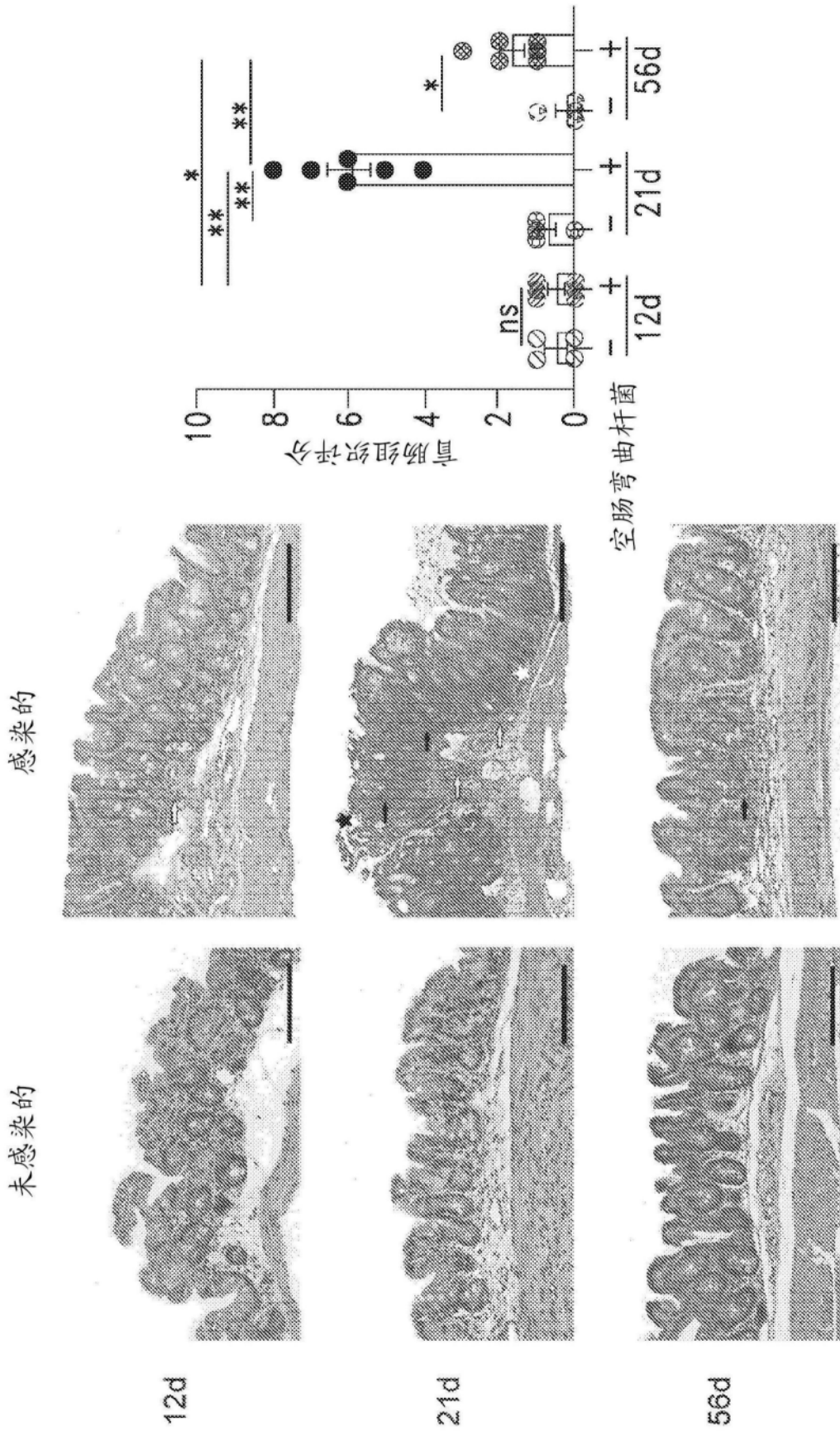


图8C

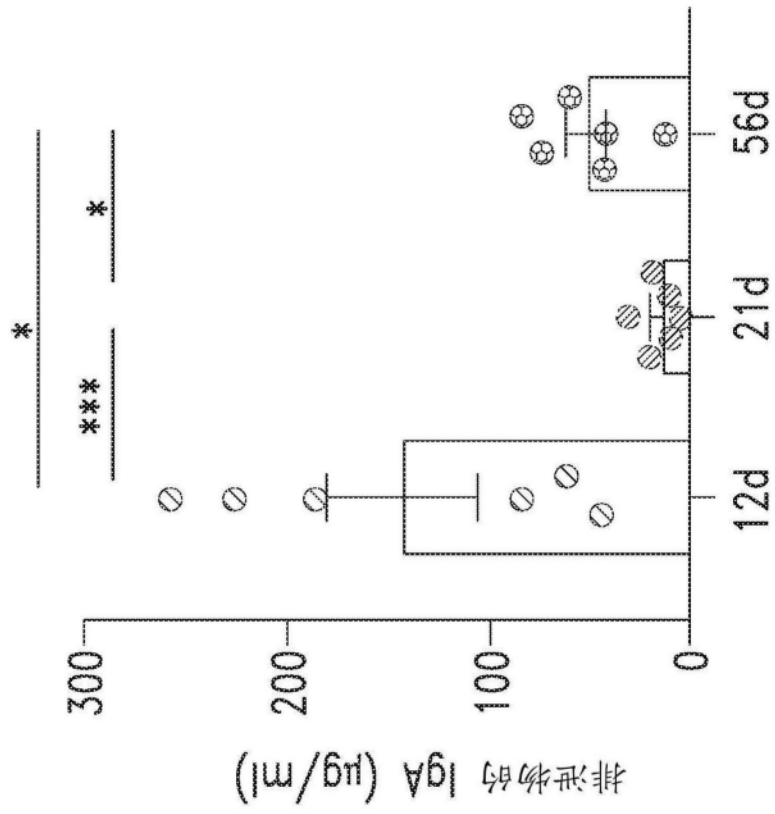


图8D

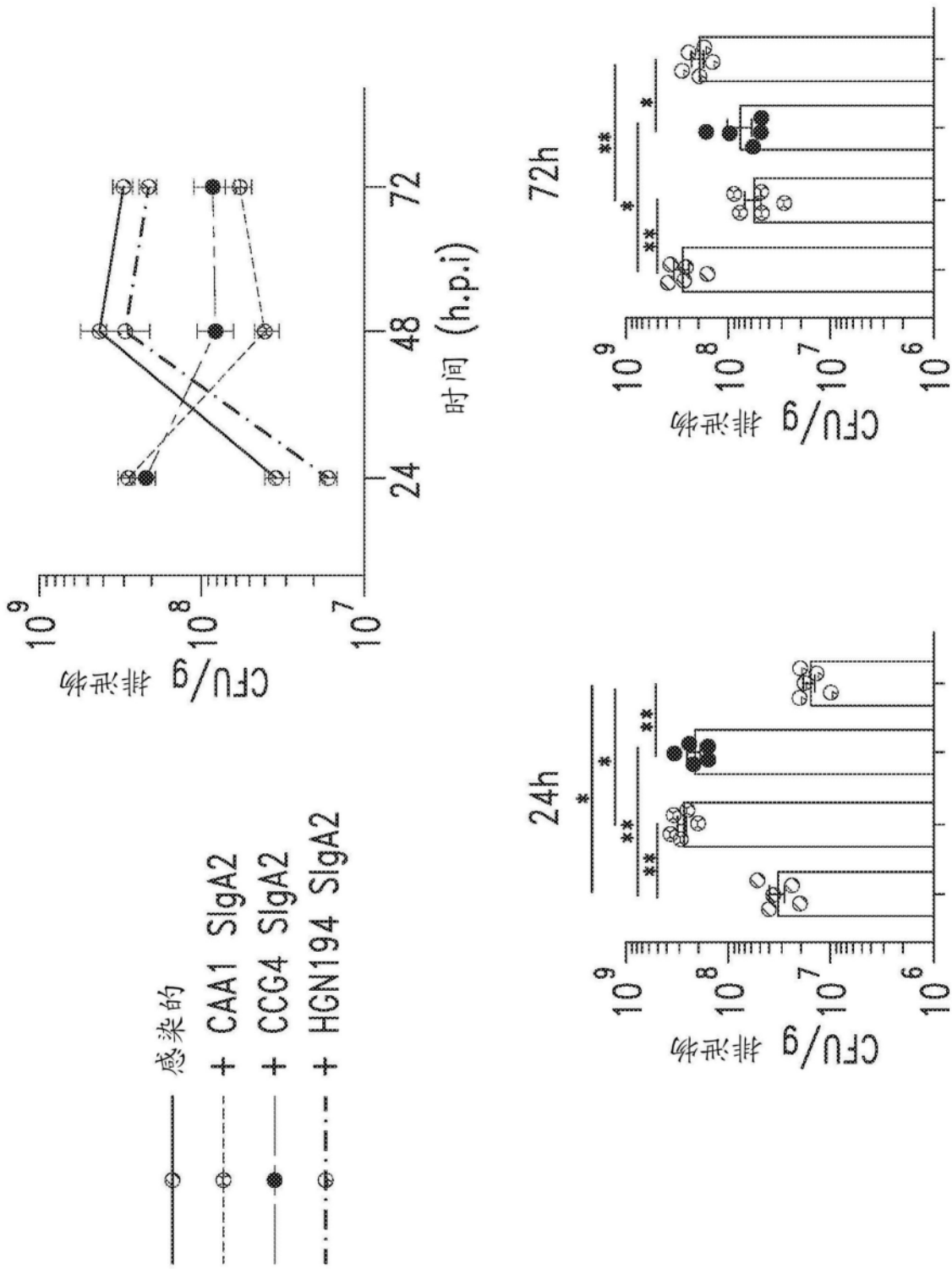


图9A

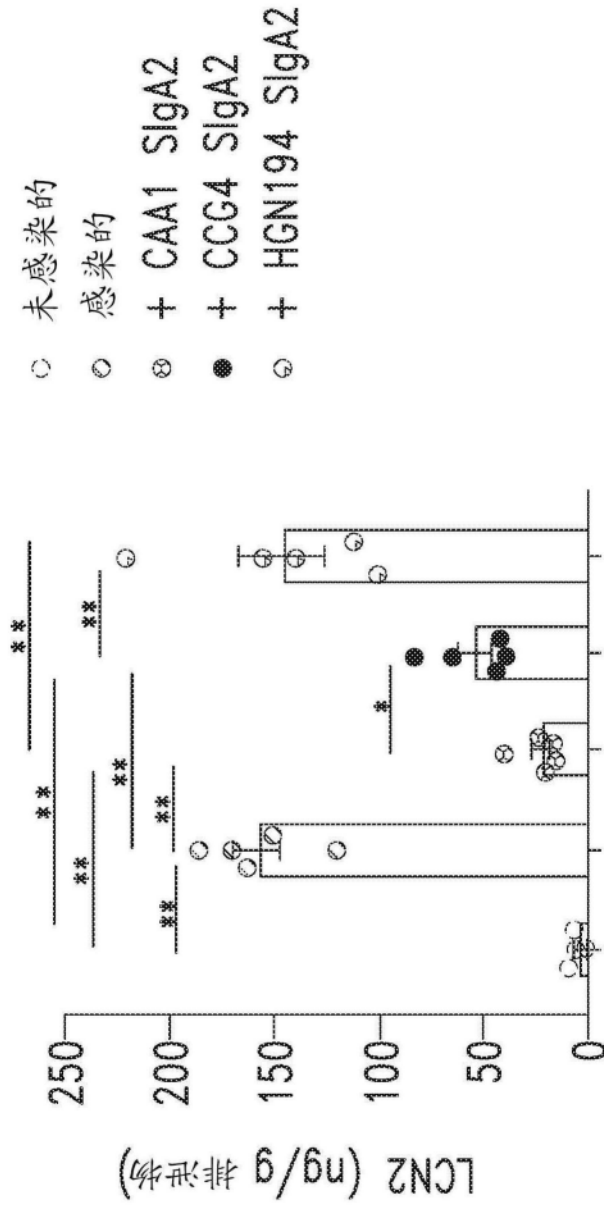


图9B

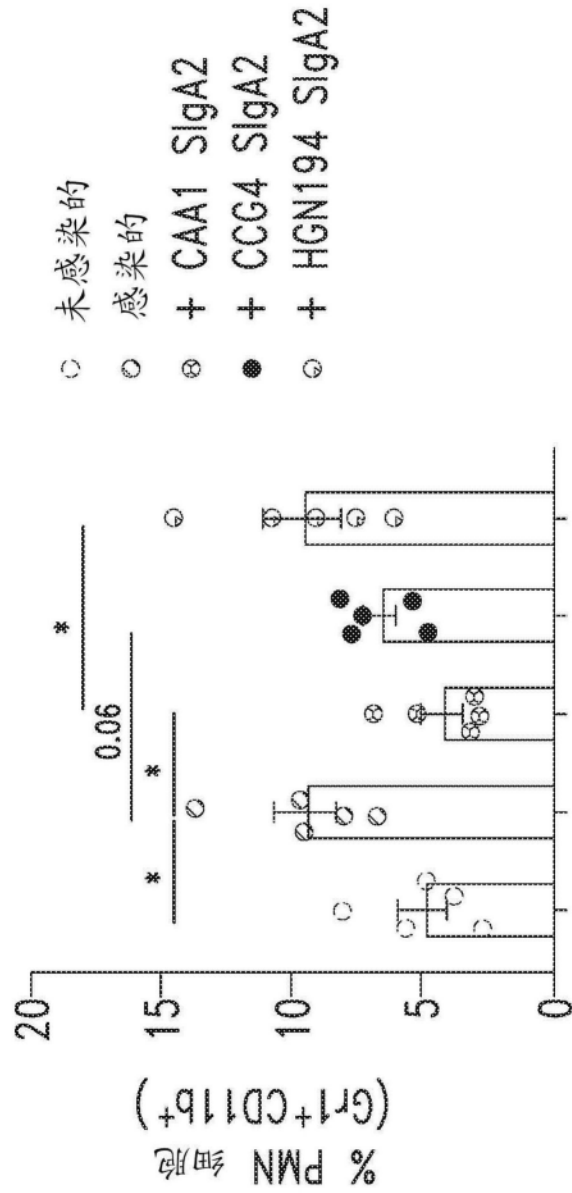


图9C

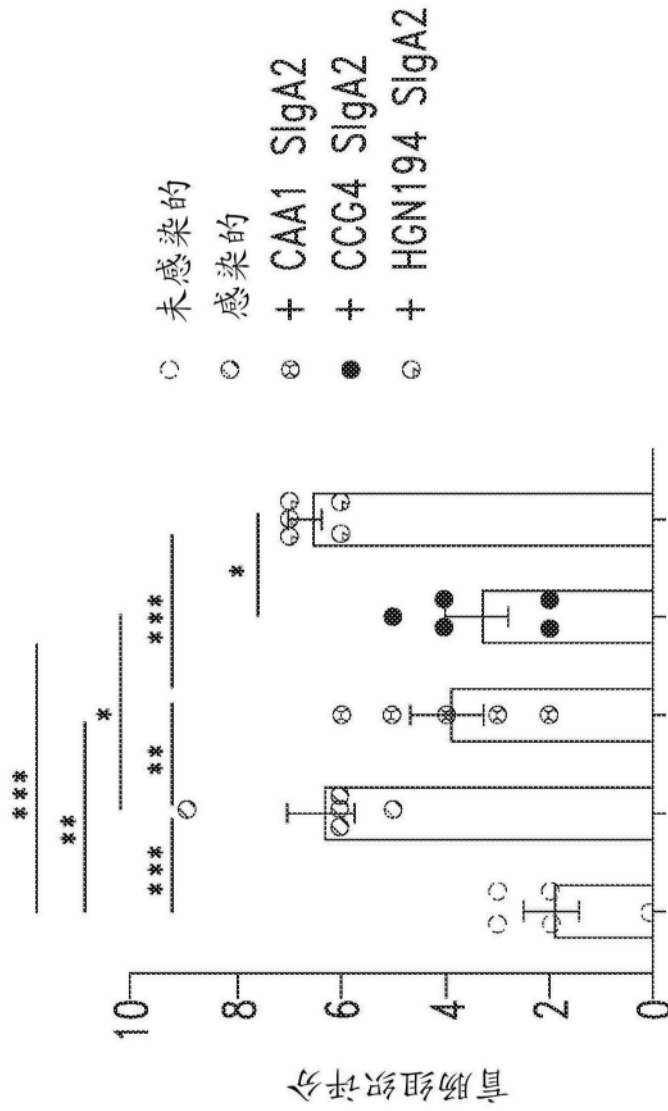


图9D

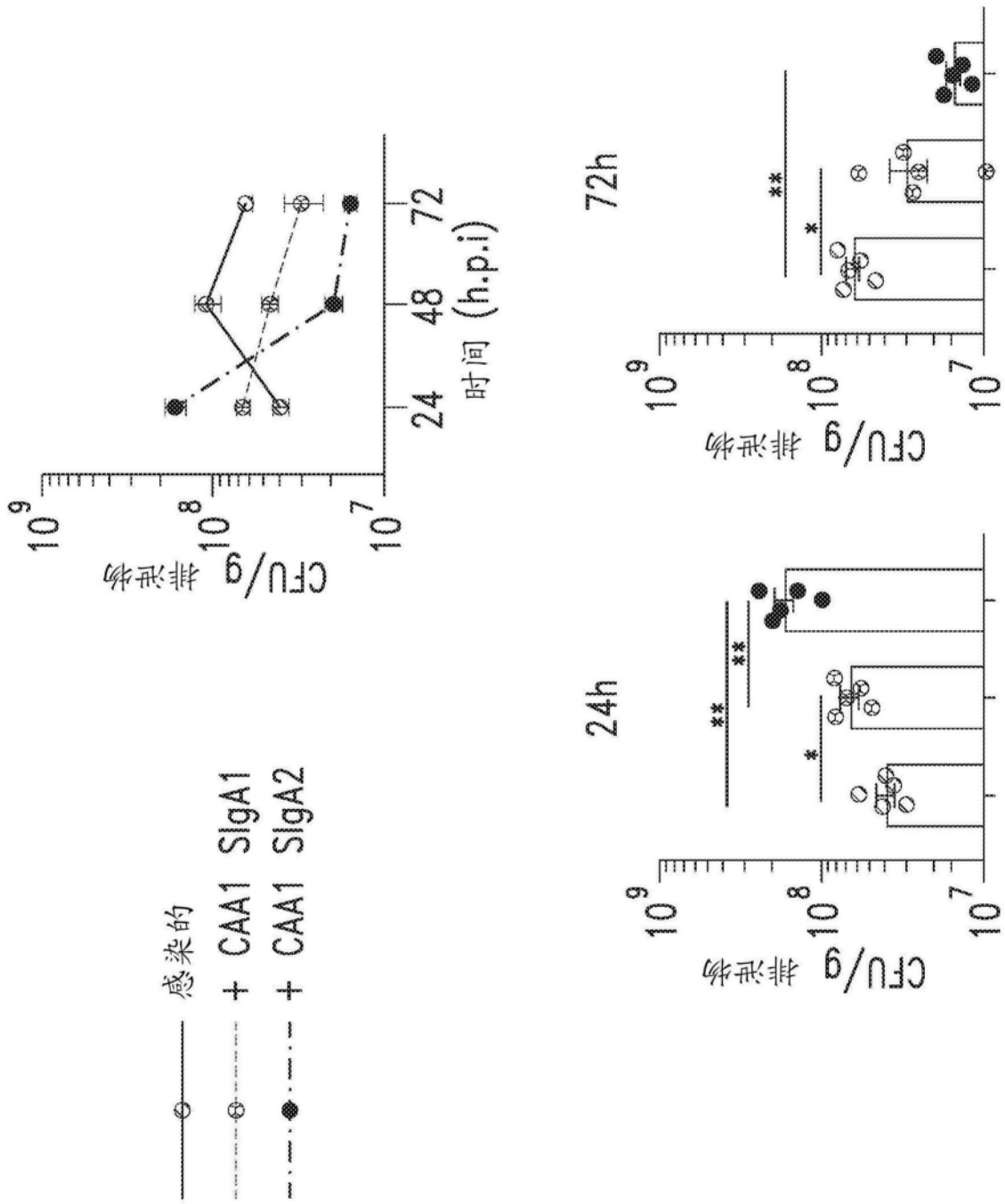


图10A

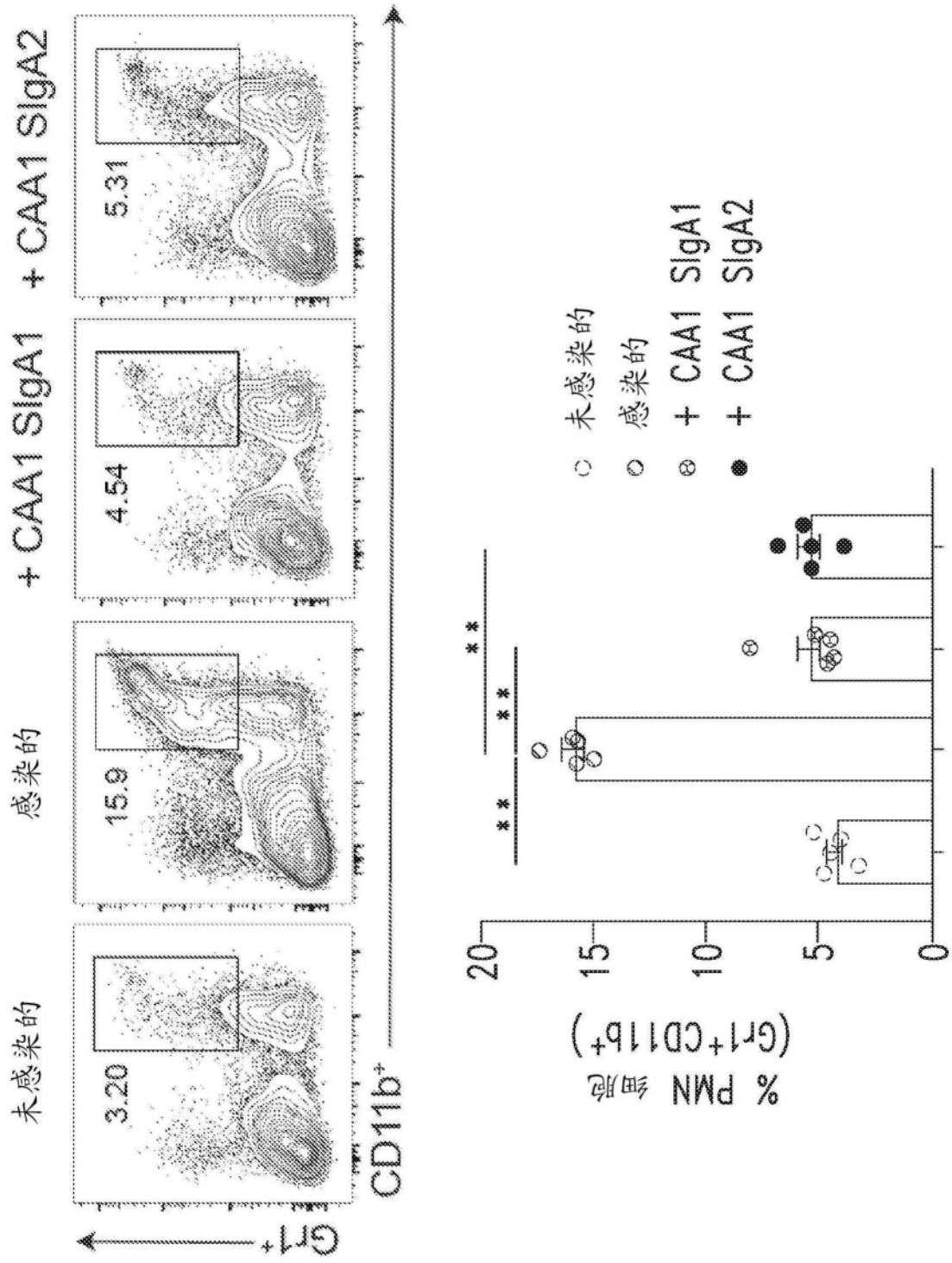


图10B

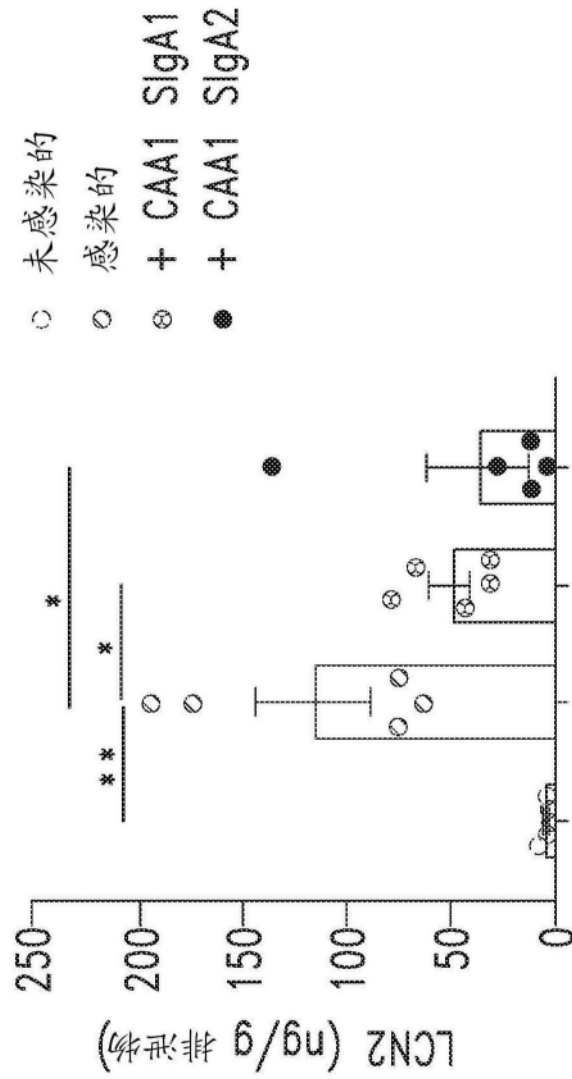


图10C

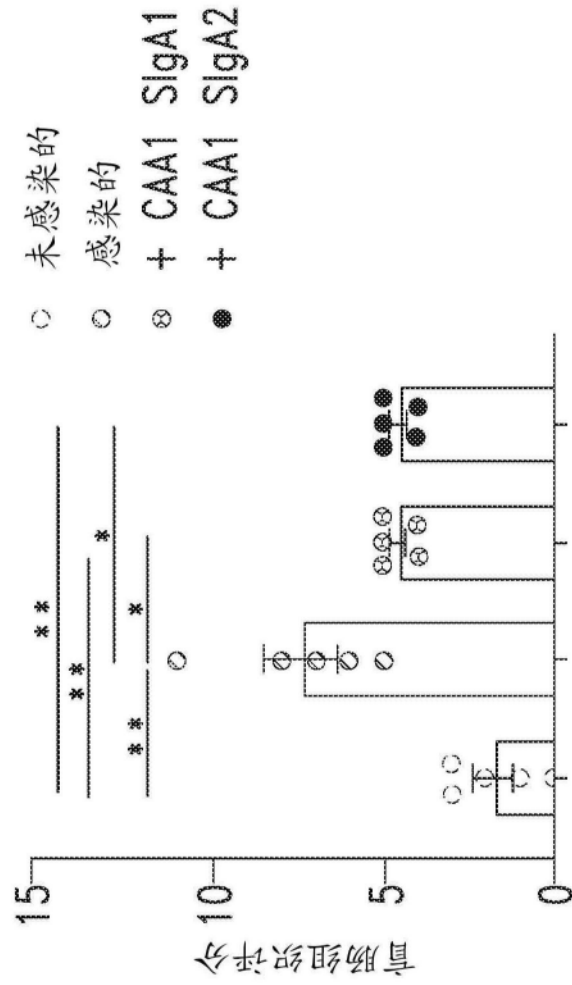


图10D

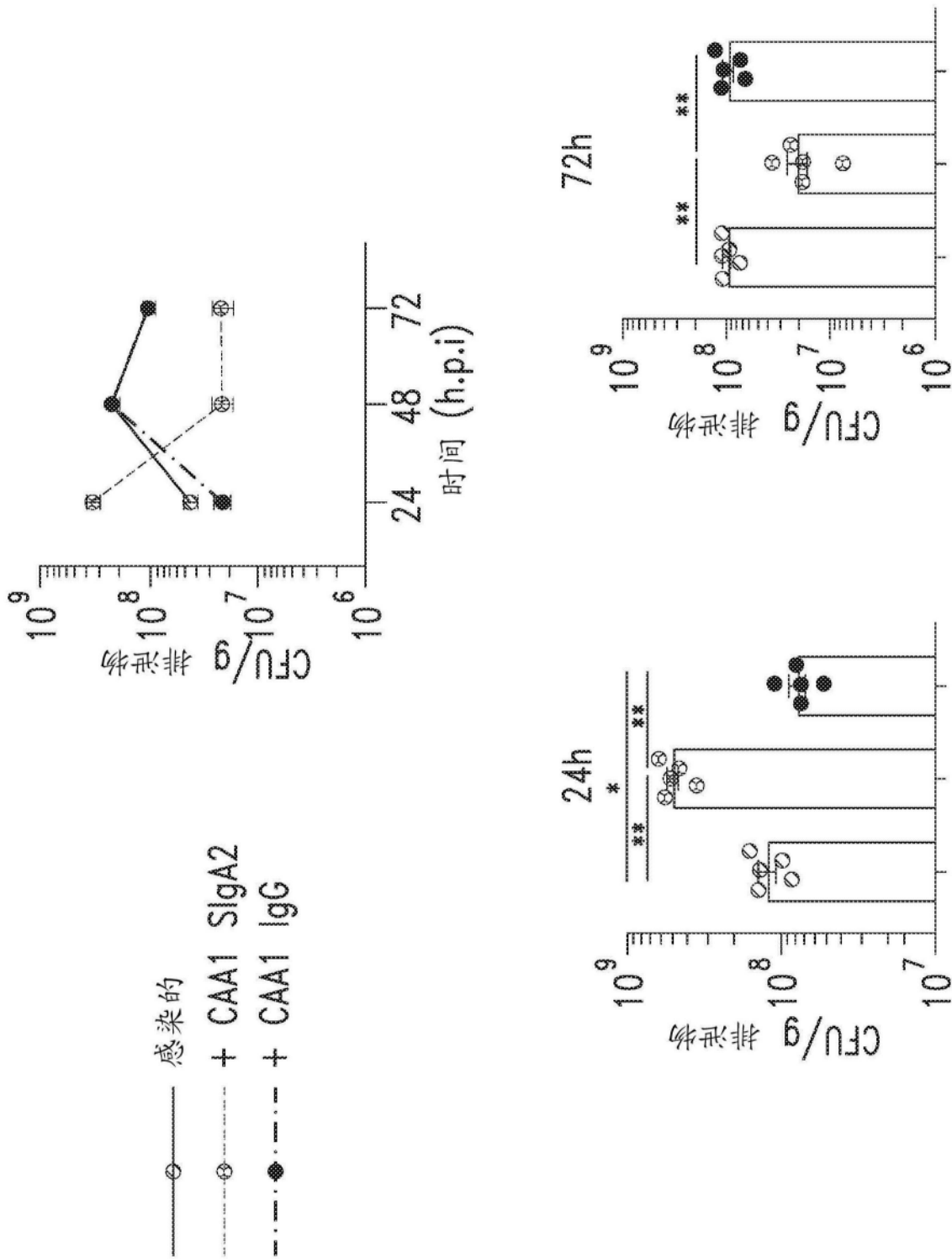


图11A

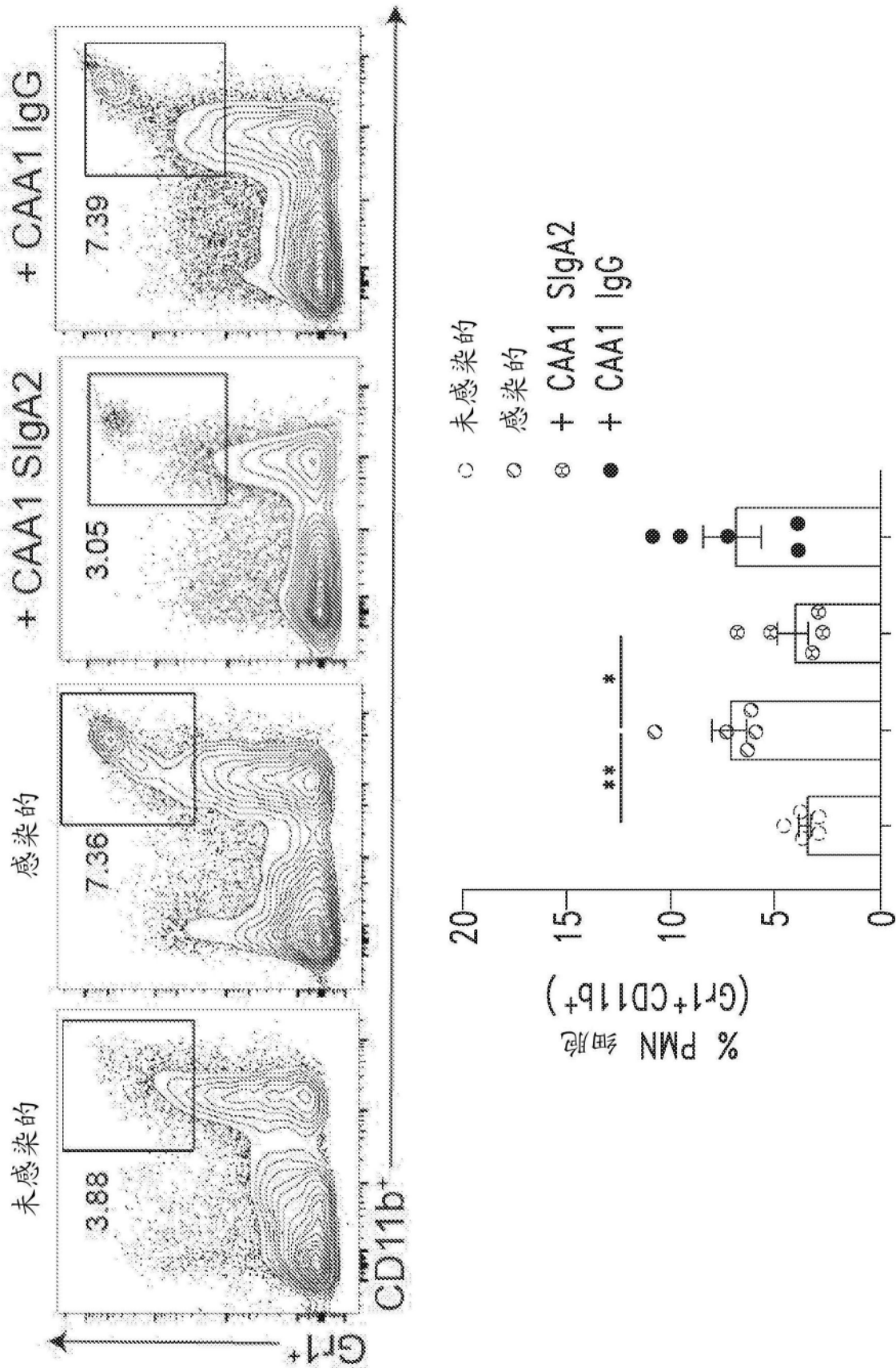


图11B

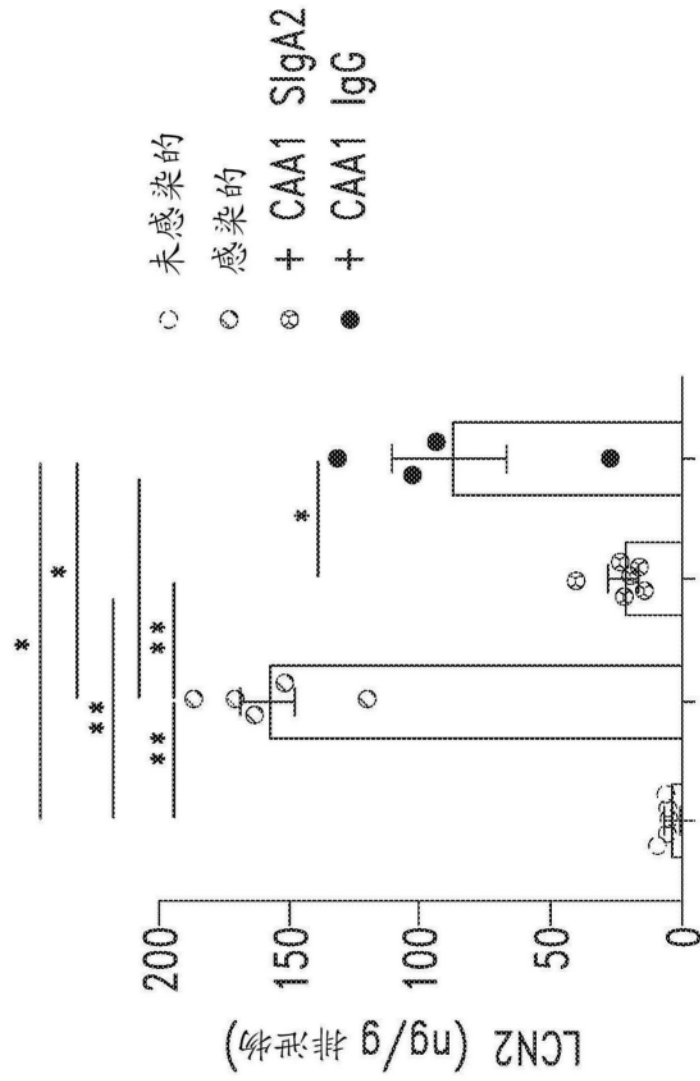


图11C

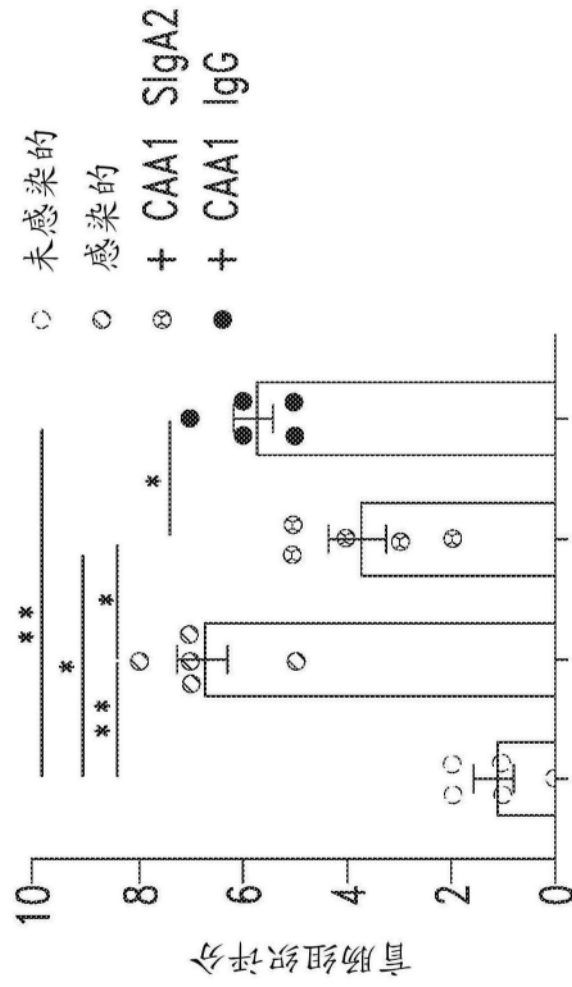


图11D

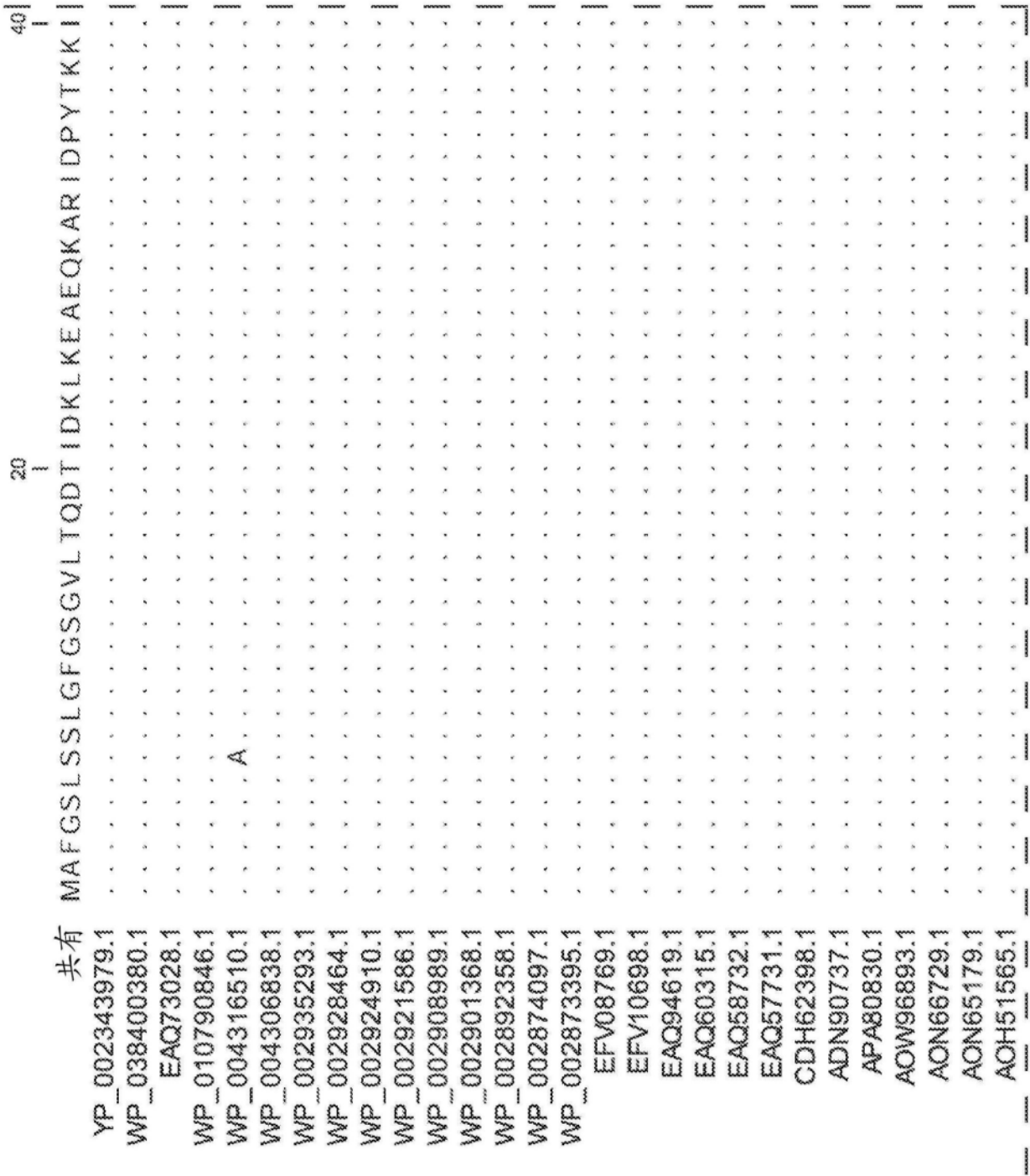


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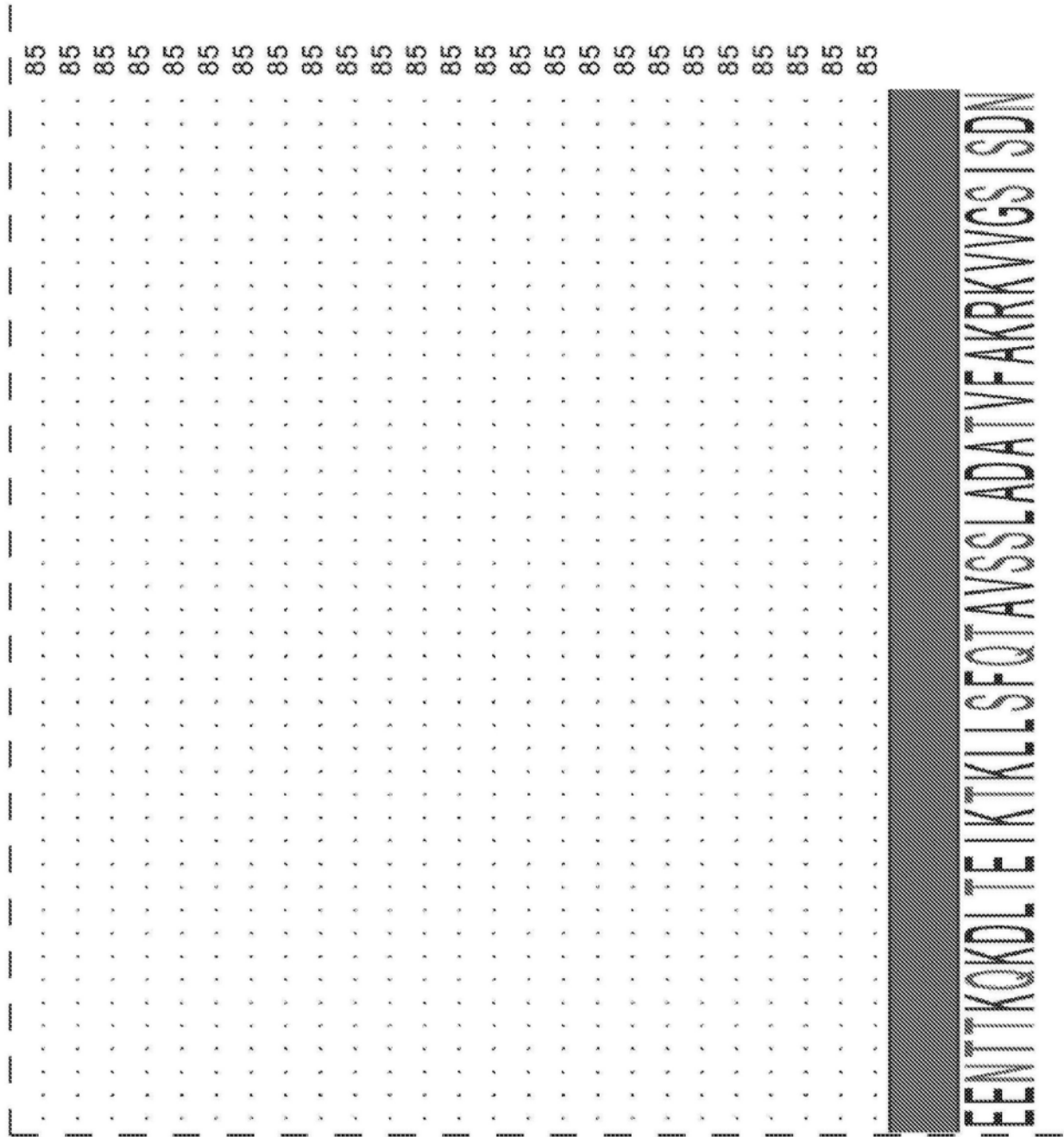


图12(续)

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WP_002928464.1Q.....
WP_002924910.1K.....
WP_002921586.1S.....I.....T.....
WP_002908989.1Q.....
WP_002901368.1S.....I.....T.....
WP_002892358.1I.....T.....
WP_002874097.1Q.....K.....
WP_002873395.1Q.....
EFV08769.1Q.....
EFV10698.1S.....T.....
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EAQ58732.1Q.....
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ADN90737.1S.....T.....
APA80830.1S.....I.....A.....
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AON66729.1Q.....K.....
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AOH51565.1Q.....

图12(续)

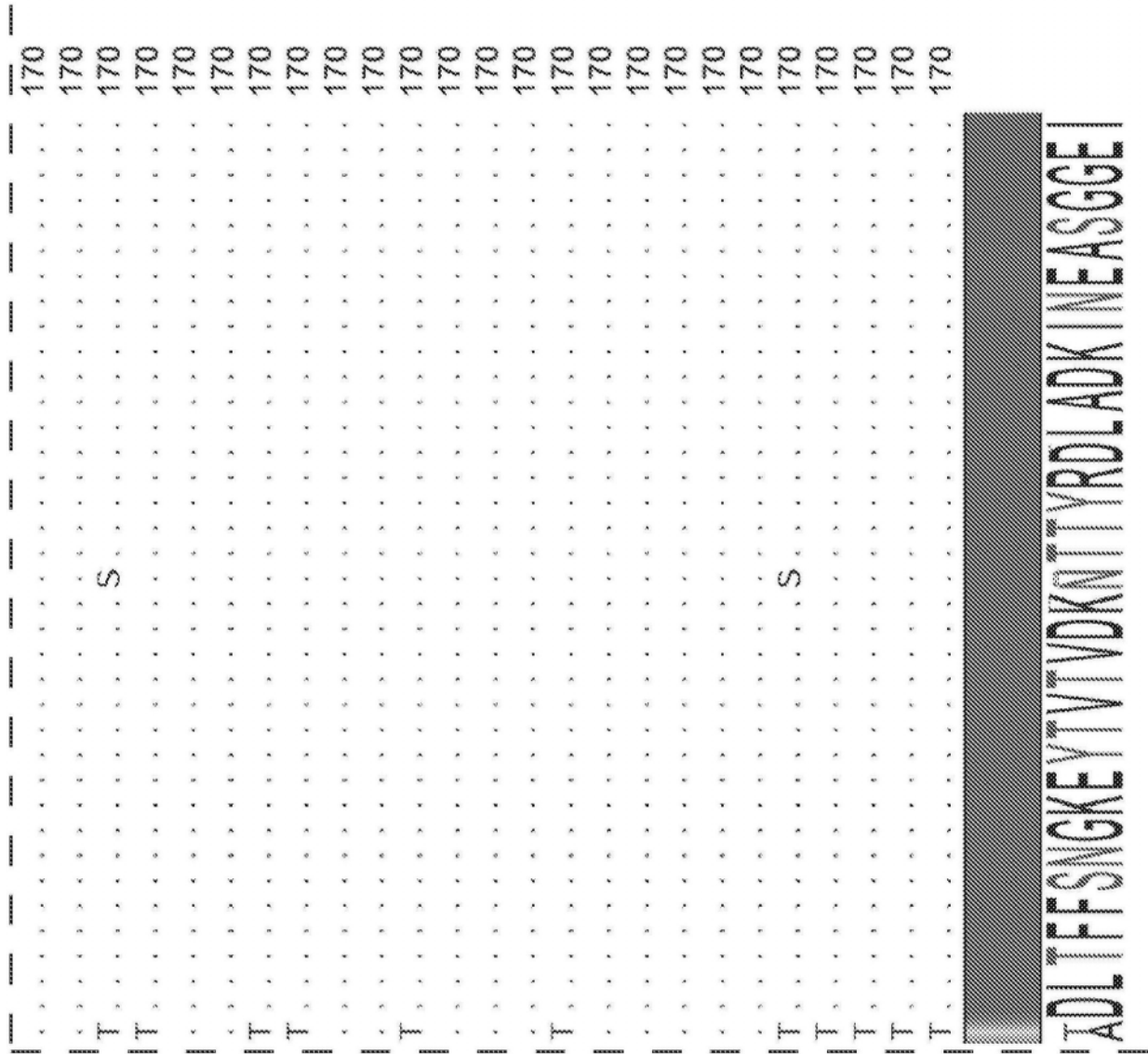


图12(续)

	180	200	220
共有	VAKI	VNTG	KGTPYRLTLTSKETGEDSAISFYAGKKDSNGKYQSDSEAEKIF
YP_002343979.1			
WP_038400380.1			K.IN
EAQ73028.1			AQ.Q.K.L
WP_010790846.1			T
WP_004316510.1			K.TN
WP_004306838.1			A.A.KN.PN
WP_002935293.1			AQ.Q.K.L
WP_002928464.1			K.TN
WP_002924910.1			K.TN
WP_002921586.1	D		VQ.Q.K
WP_002908989.1			T
WP_002901368.1			K.TN
WP_002892358.1			T.L.KT
WP_002874097.1			A.KN.PN
WP_002873395.1			AQ.Q.K
EFV08769.1			K.TN
EFV10698.1			K.IN
EAQ94619.1			AQ.Q.P
EAQ60315.1			AQ.Q.P
EAQ58732.1			AQ.Q.K
EAQ57731.1			K.TN
CDH62398.1			K.IN
ADN90737.1			AQ.Q.K
APA80830.1			AQ.Q.P
AOW96893.1			AQ.Q.P
AON66729.1			AQ.Q.K
AON65179.1			AQ.Q.K
AOH51565.1			AQ.Q.P
			Q
			N

图12(续)

240
┆

KNL	GWELDKTT - SIDPAKDKKGYG	IKDASLHIQ	254
DD	G VSA - D		254
S	S		254
	T S		254
DD	G ASA -		254
	A S L	T	254
S	S		254
DD	VSA - D		254
DD	G ASA -		254
S	S		254
	T S		254
DD	G VSA - D		254
	T S		254
	T QT		255
S	S	S	254
DD	G VSA -		254
DD	G VSA - D		254
S	QT		255
S	QT		255
S	QT		255
DD	G ASA -		254
DD	G VSA - D		254
S	S		254
S	QT		255
S	QT		255
S	QT		255
S	S		254
S	QT		255
S	S		254

图12(续)

	260	280
	TAQNAEFTLDGIKMFRSSNTVTDLGVGMTLTLNKGTGEINF	
共有		
YP_002343979.1		
WP_038400380.1		
EAQ73028.1		
WP_010790846.1		
WP_004316510.1		
WP_004306838.1		
WP_002935293.1		
WP_002928464.1		
WP_002924910.1		
WP_002921586.1		
WP_002908989.1		
WP_002901368.1		
WP_002892358.1		
WP_002874097.1		
WP_002873395.1		
EFV08769.1		
EFV10698.1		
EAQ84619.1		
EAQ60315.1		
EAQ58732.1		
EAQ57731.1		
CDH62398.1		
ADN90737.1		
APA80830.1		
AOW96893.1		
AON66729.1		
AON65179.1		
AOH51565.1		

图12(续)

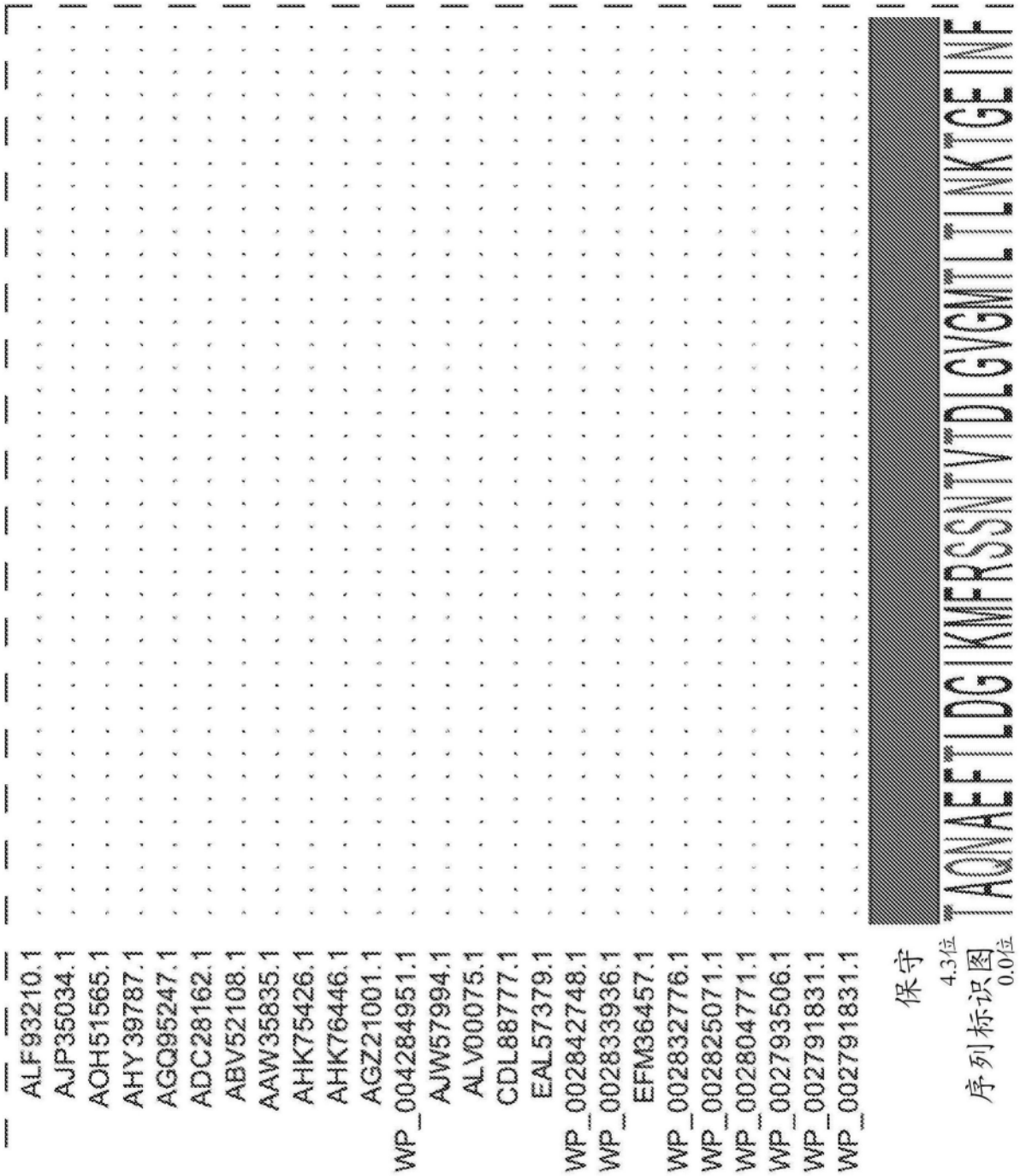


图12(续)

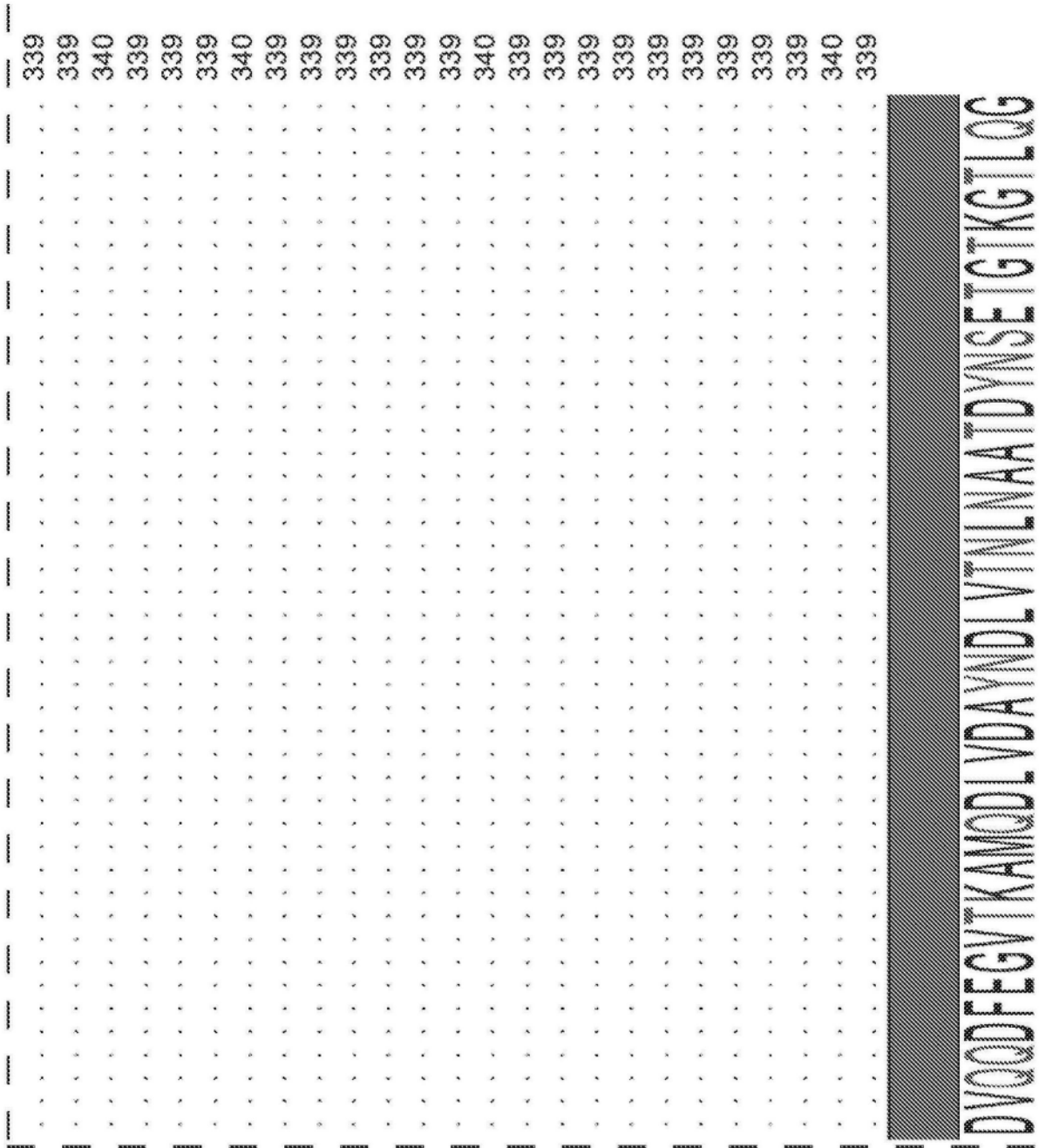


图12(续)

	360	ISEVNSIRSSI LADLFDSQVVDGTTEDANGNKVNTKVMLSMQD
共有		
YP_002343979.1		
WP_038400380.1		
EAQ73028.1		
WP_010790846.1		
WP_004316510.1		
WP_004306838.1		
WP_002935293.1		
WP_002928464.1		
WP_002924910.1		
WP_002921586.1		
WP_002908989.1		
WP_002901368.1		
WP_002892358.1		
WP_002874097.1		
WP_002873395.1		
EFV08769.1		
EFV10698.1		
EAQ94619.1		
EAQ60315.1		
EAQ58732.1		
EAQ57731.1		
CDH62398.1		
ADN90737.1		
APA80830.1		
AOW96893.1		
AON66729.1		
AON65179.1		
AOH51565.1		

图12(续)

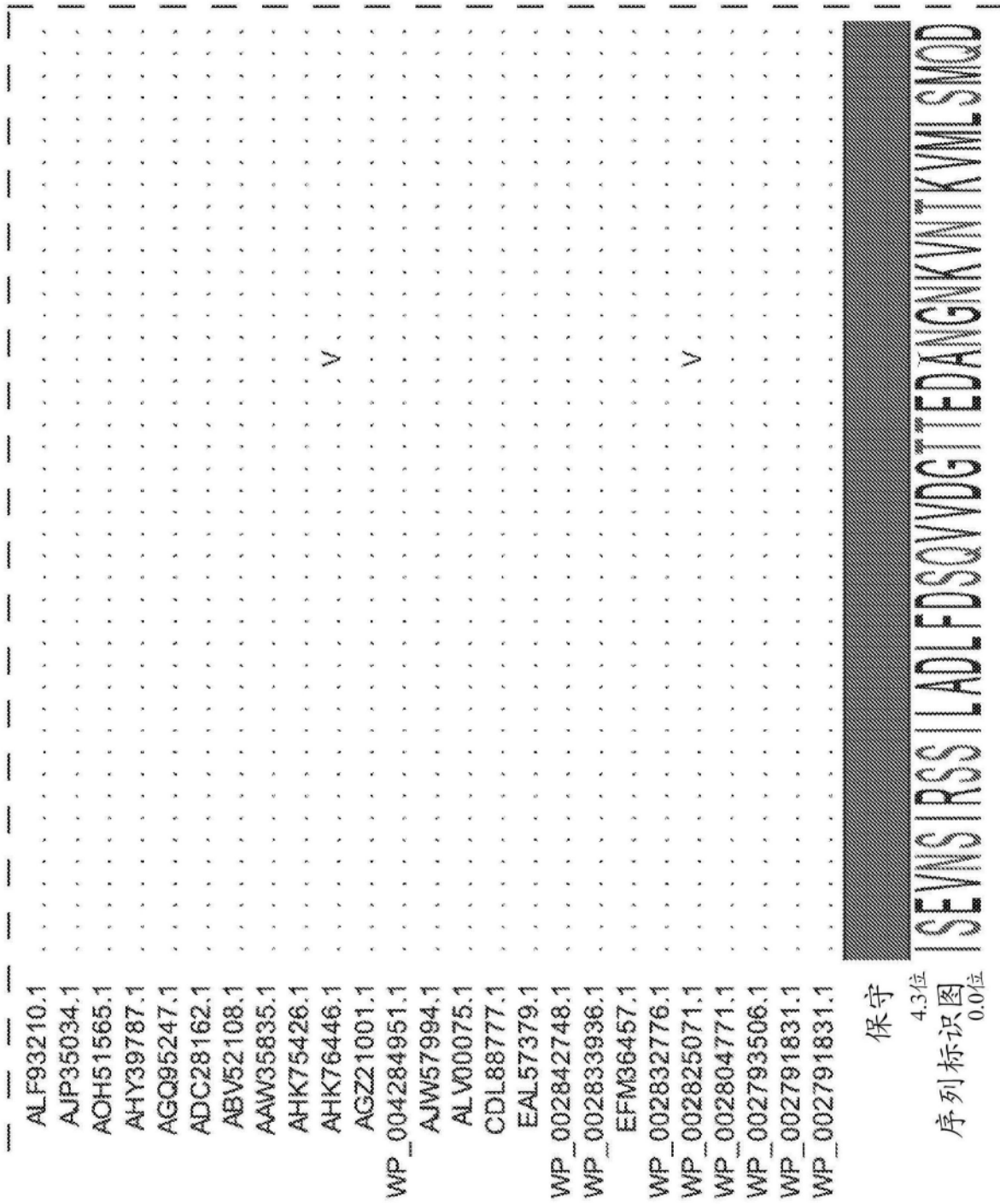


图12(续)

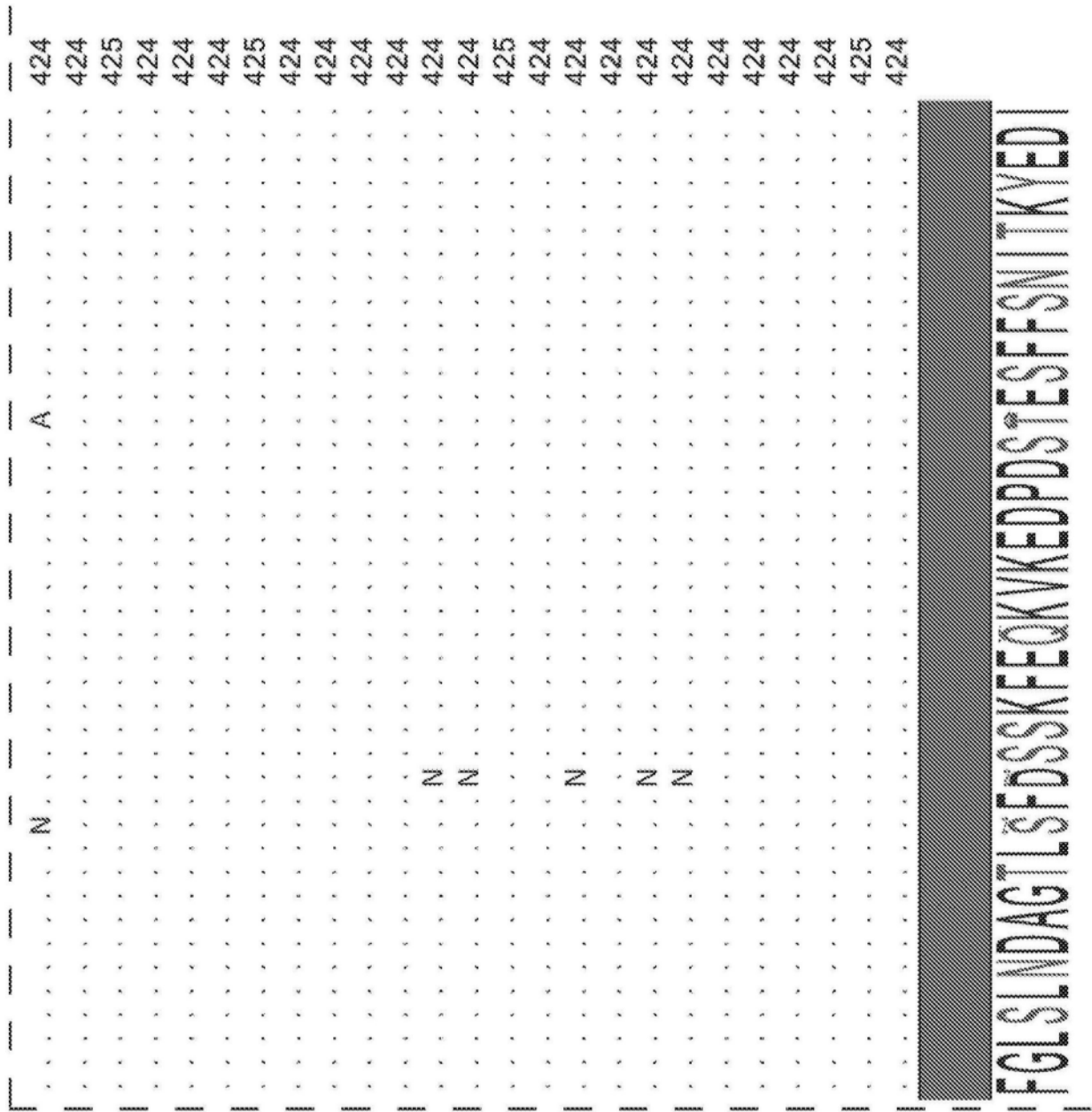


图12(续)

	440	460
共有	NHTGEVIKTSLSKYLNSNGGNTNGLEFKPGDFTIVFNNQTYDL	
YP_002343979.1		
WP_038400380.1		A
EAQ73028.1	Q . . . NQ . . D . S . TGNK . . D	D
WP_010790846.1		
WP_004316510.1		
WP_004306838.1		SA . . D
WP_002935293.1		Y
WP_002928464.1		D
WP_002924910.1		
WP_002921586.1	Q . . . NQ . . D . S . TGNK . . D	
WP_002908989.1	Q . . . NQ . . D . S . TGNK . . D	
WP_002901368.1	Q . . . NQ . . D . S . TGNK . . D	
WP_002892358.1	Q . . . NQ . . D . S . TGNK . . D	
WP_002874097.1		
WP_002873395.1		
EFV08769.1		
EFV10698.1	Q . . . NQ . . D . S . TGNK . . D	
EAQ94619.1		
EAQ60315.1	Q . . . NQ . . D . S . TGNK	G
EAQ58732.1	I . . . N .	D
EAQ57731.1		
CDH62398.1		
ADN90737.1	Q . . . NQ . . D . S . TGNK . . D	
APA80830.1		
AOW96893.1	Q . . . NQ . . D . S . TGNK	G
AON66729.1		
AON65179.1		A
AOH51565.1	N .	P D

图12(续)

ALF93210.1	I . . . N	D
AJP35034.1
AOH51565.1	Q . . . NQ . D . S . TGNK	Q . N
AHY39787.1	A
AGQ95247.1
ADC28162.1
ABV52108.1	Q . . . NQ . D . S . TGNK	D
AAW35835.1
AHK75426.1
AHK76446.1	N	P
AGZ21001.1	D
WP_004284951.1
AJW57994.1
ALV00075.1
CDL88777.1	Q . . . NQ . D . S . TGNK	D
EAL57379.1
WP_002842748.1
WP_002833936.1
EFM36457.1
WP_002832776.1
WP_002825071.1
WP_002804771.1	N
WP_002793506.1
WP_002791831.1	Q . . . NQ . D . S . TGNK	D
WP_002791831.1
保守		
序列标识图		
4.3位		
0.0位		
NHTGEVIK ⁹ GSLSRYLRS ⁵ NG ⁹ YKGL ⁹ EFKPG ⁵ FTVFMQTYDL		

图12(续)

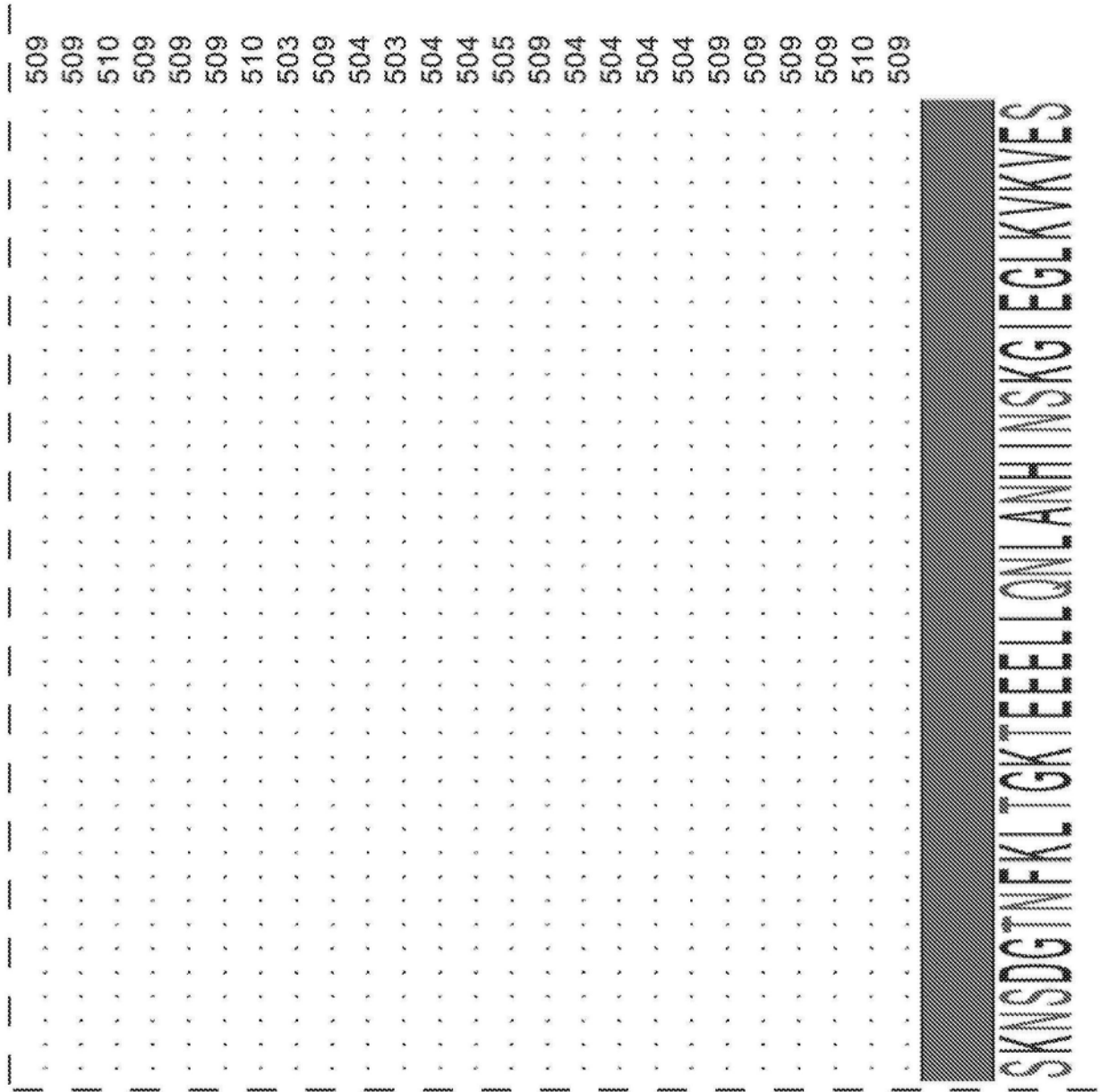


图12(续)

ALF93210.1	D . . . K . . K	S	I
AJP35034.1	D . . G . K D
AOH51565.1	D . . G . K . . K
AHY39787.1 GS
AGQ95247.1
ADC28162.1
ABV52108.1	D . . G . K . . K	N . T . Q
AAW35835.1 N . S
AHK75426.1
AHK76446.1	. . . G . K . . K	N . S
AGZ21001.1 N . S
WP_004284951.1 N . S
AJW57994.1 N . S
ALV00075.1 N . S
CDL88777.1	D . . G . K . . K	N . T
EAL57379.1 N . S
WP_002842748.1 N . S S
WP_002833936.1 N . S
EFM36457.1 N . S
WP_002832776.1 N . S
WP_002825071.1 N . S
WP_002804771.1 N . S
WP_002793506.1 S
WP_002791831.1	D . . G . K . . K	N . T . Q
WP_002791831.1 S
保留			
序列标识图			
4.3位			
0.0位			
YRQMNVPGRLNFSGDGSDFSIKGBANLRELGLSDVNI TSKP			

图12(续)

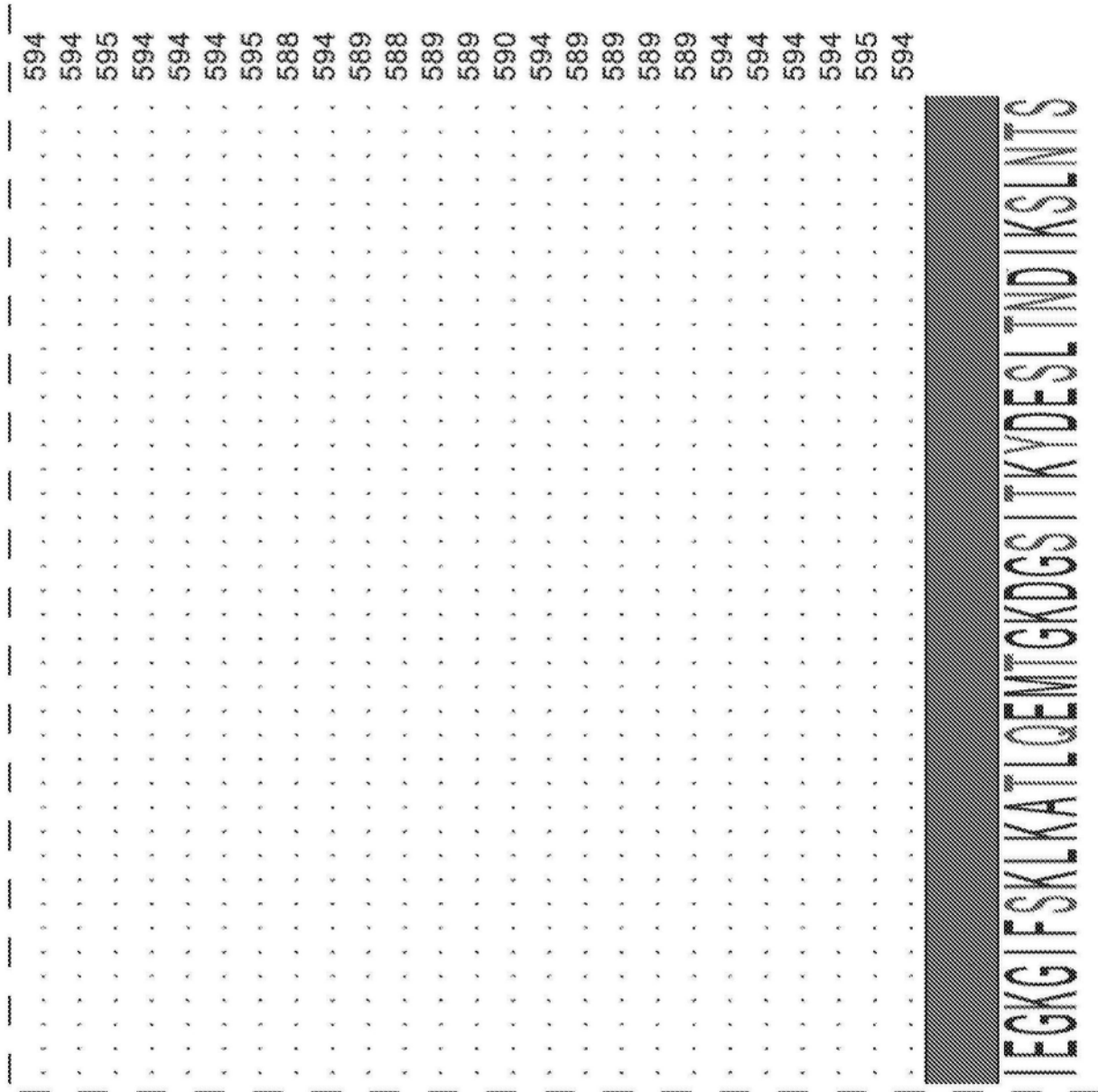


图12(续)

ALF93210.1
AJP35034.1
AOH51565.1
AHY39787.1
AGQ95247.1
ADC28162.1
ABV52108.1
AAW35835.1
AHK75426.1
AHK76446.1
AGZ21001.1
WP_004284951.1
AJW57994.1
ALV00075.1
CDL88777.1
EAL57379.1
WP_002842748.1
WP_002833936.1
EFM36457.1
WP_002832776.1
WP_002825071.1
WP_002804771.1
WP_002793506.1
WP_002791831.1
WP_002791831.1
保留
序列标识图
4.3位
0.0位
KDSTQAMIDTRYDTMANGWLQESIL

图12(续)

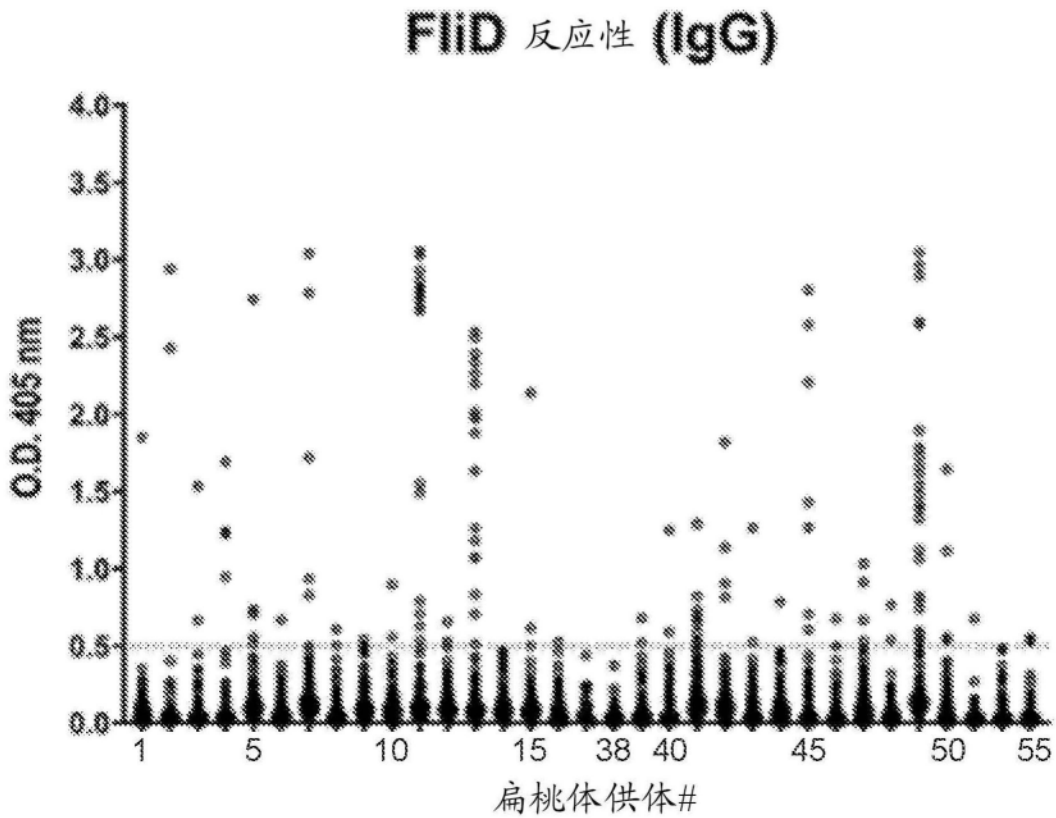
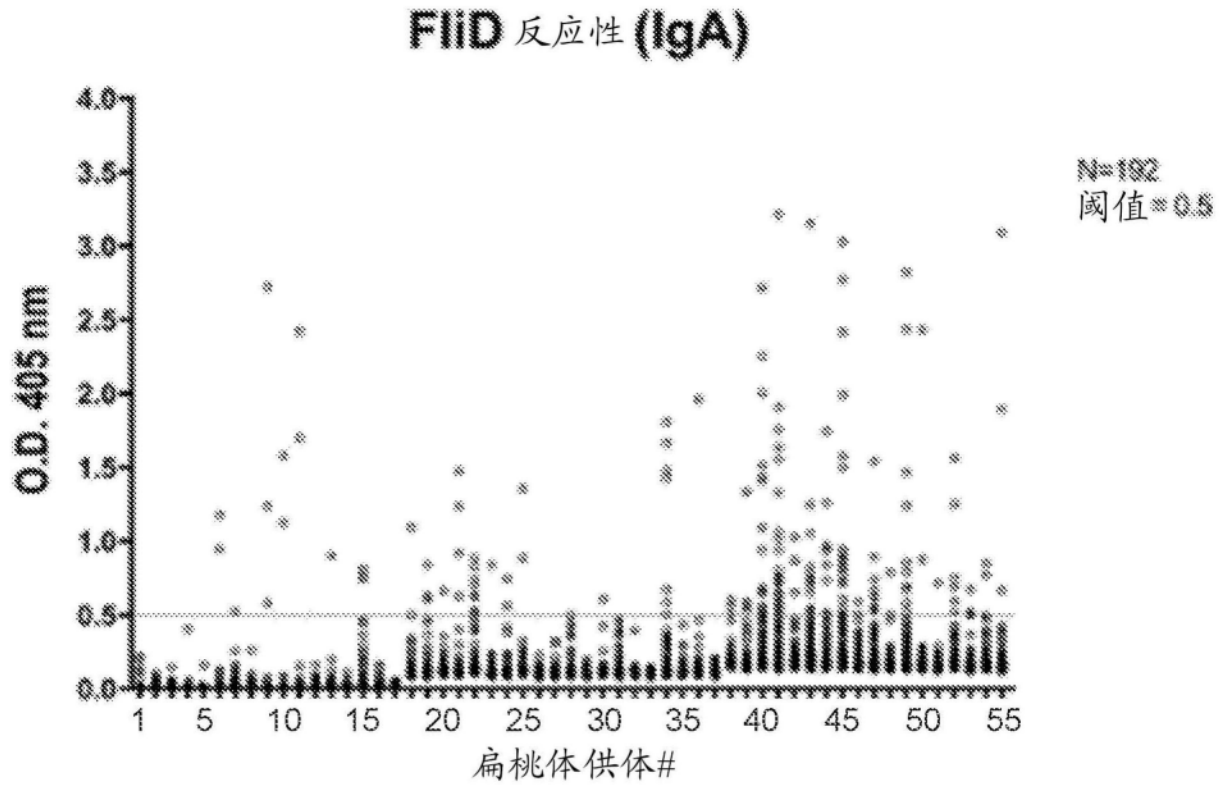


图13

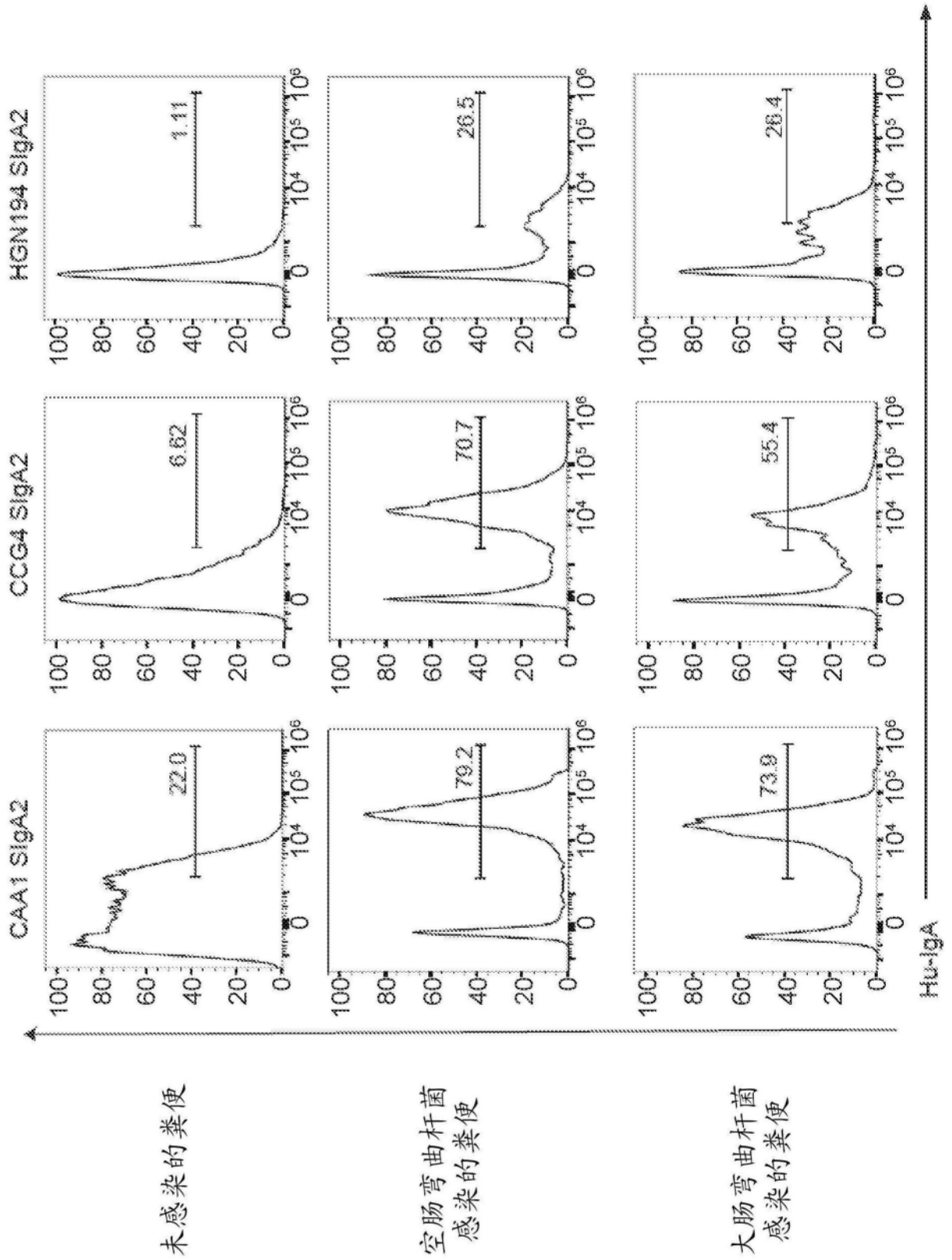


图14A

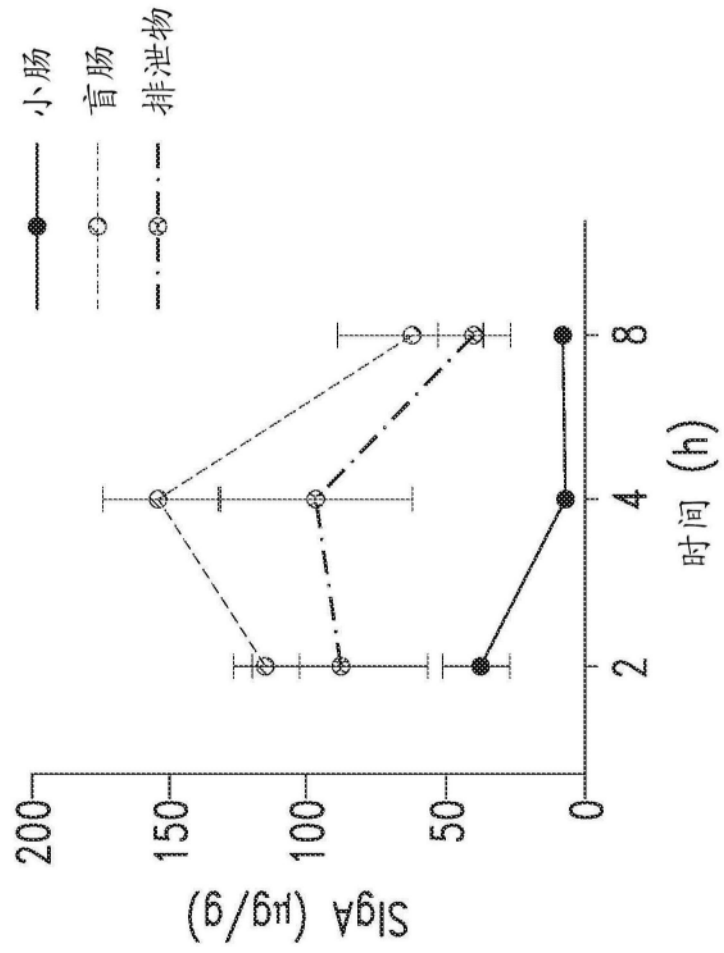


图14B

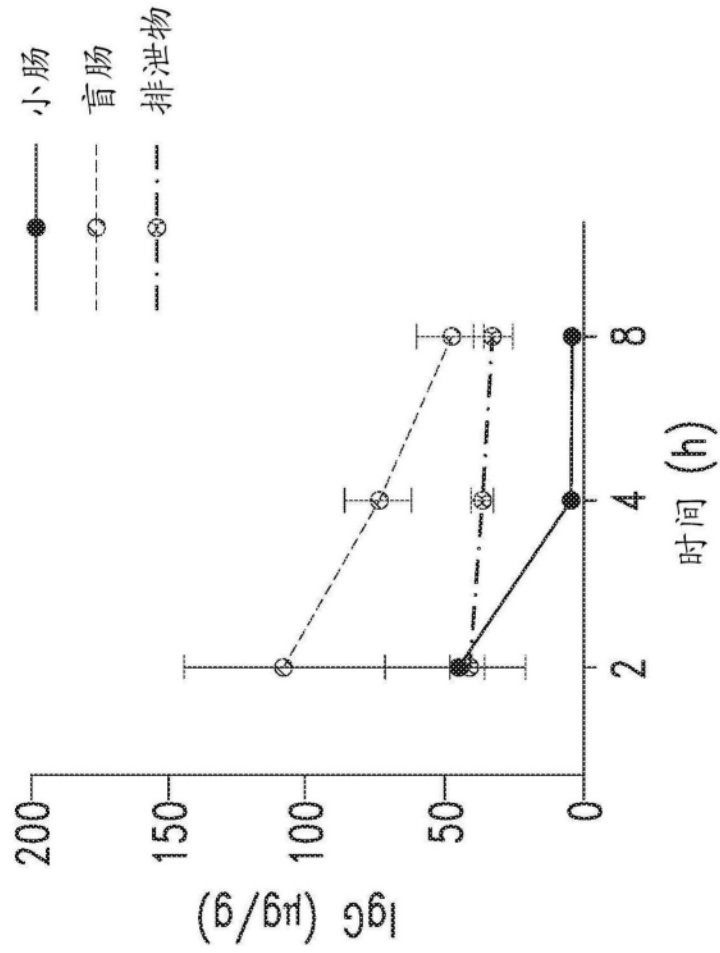


图14C

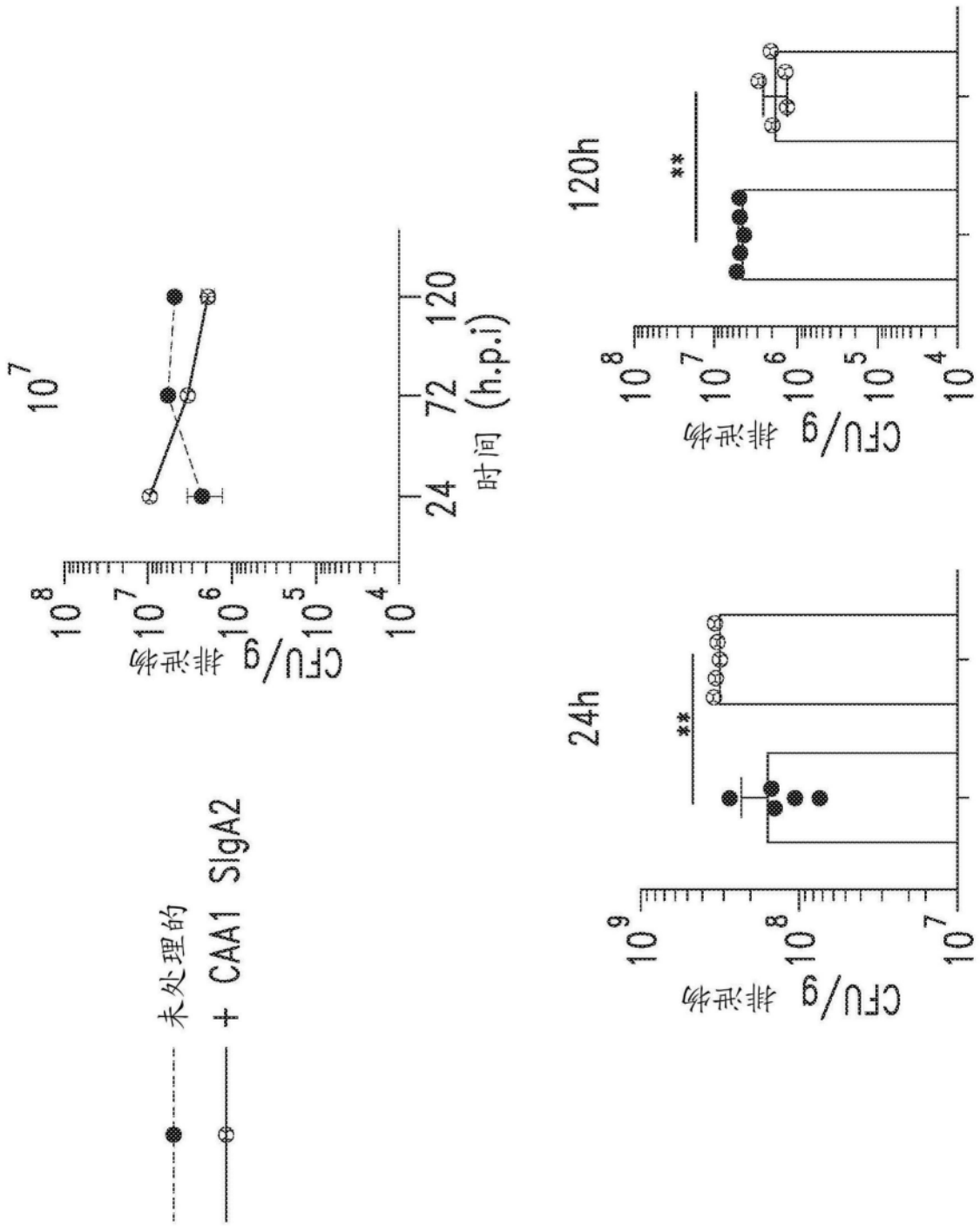


图15A

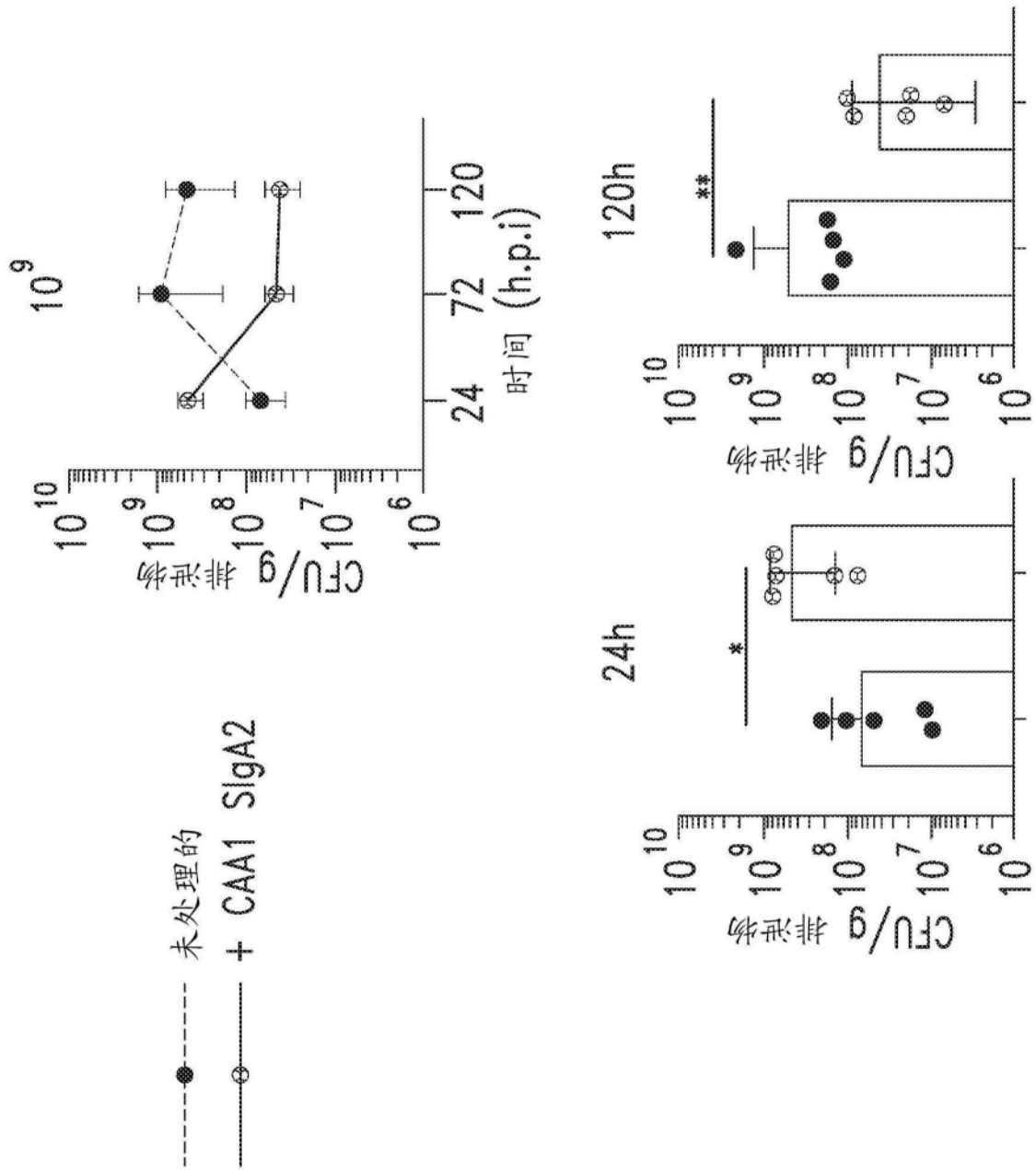


图15B

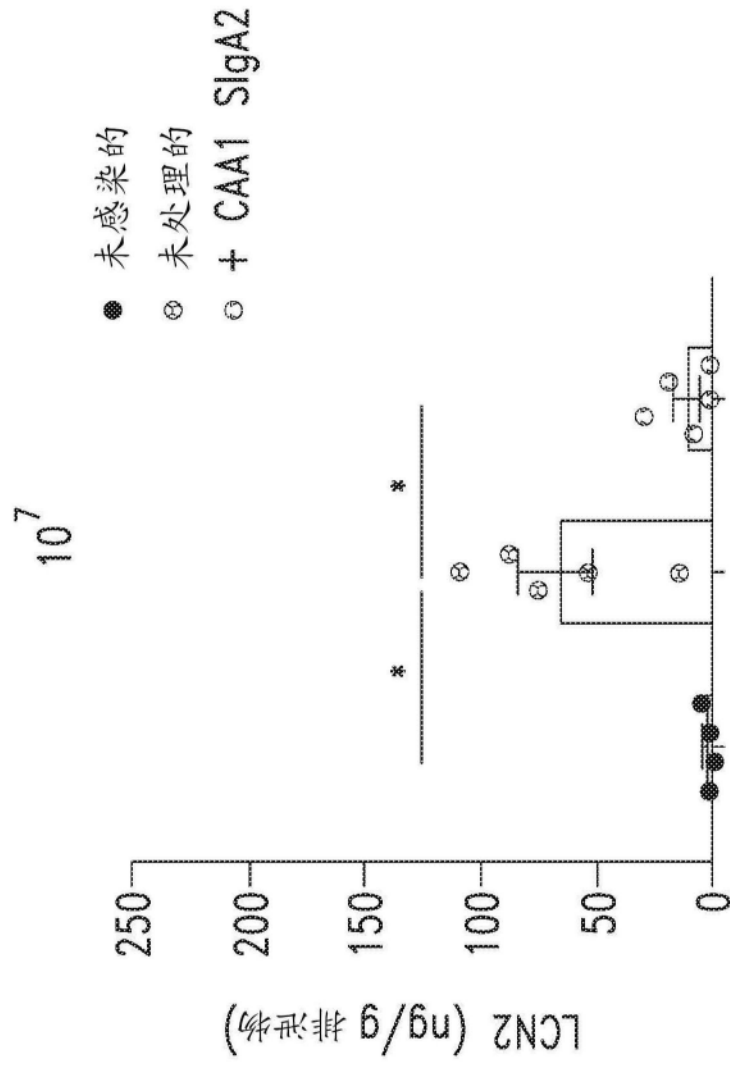


图15C

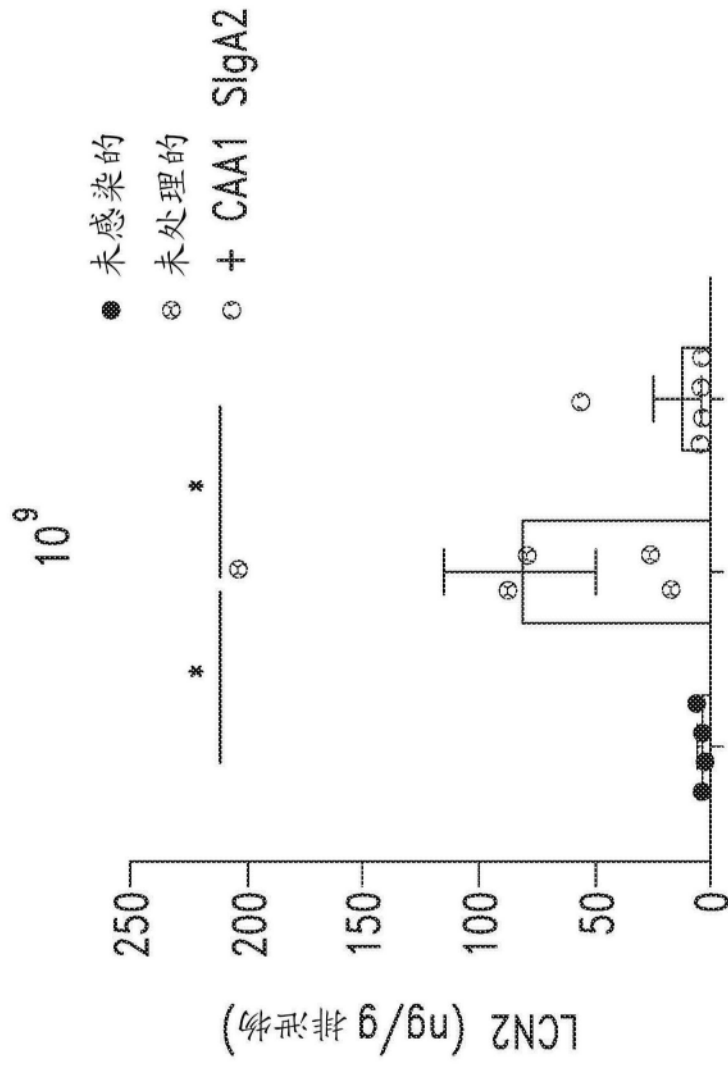


图15D

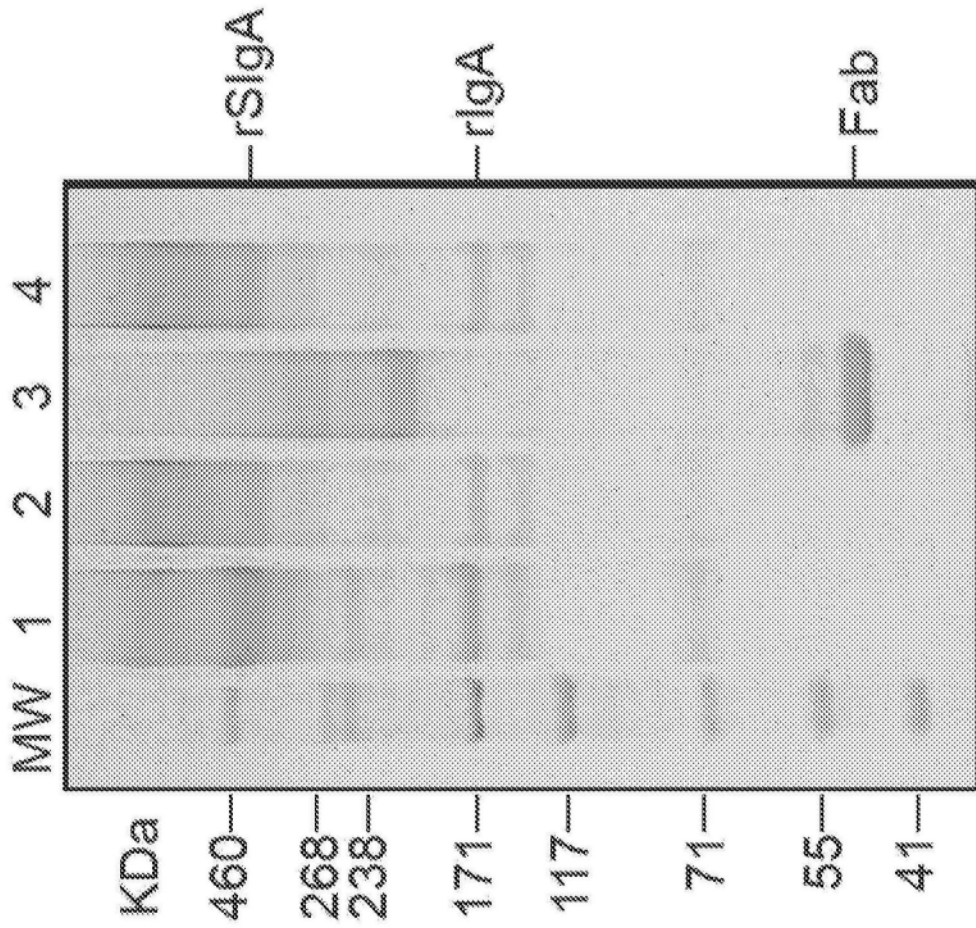


图16A

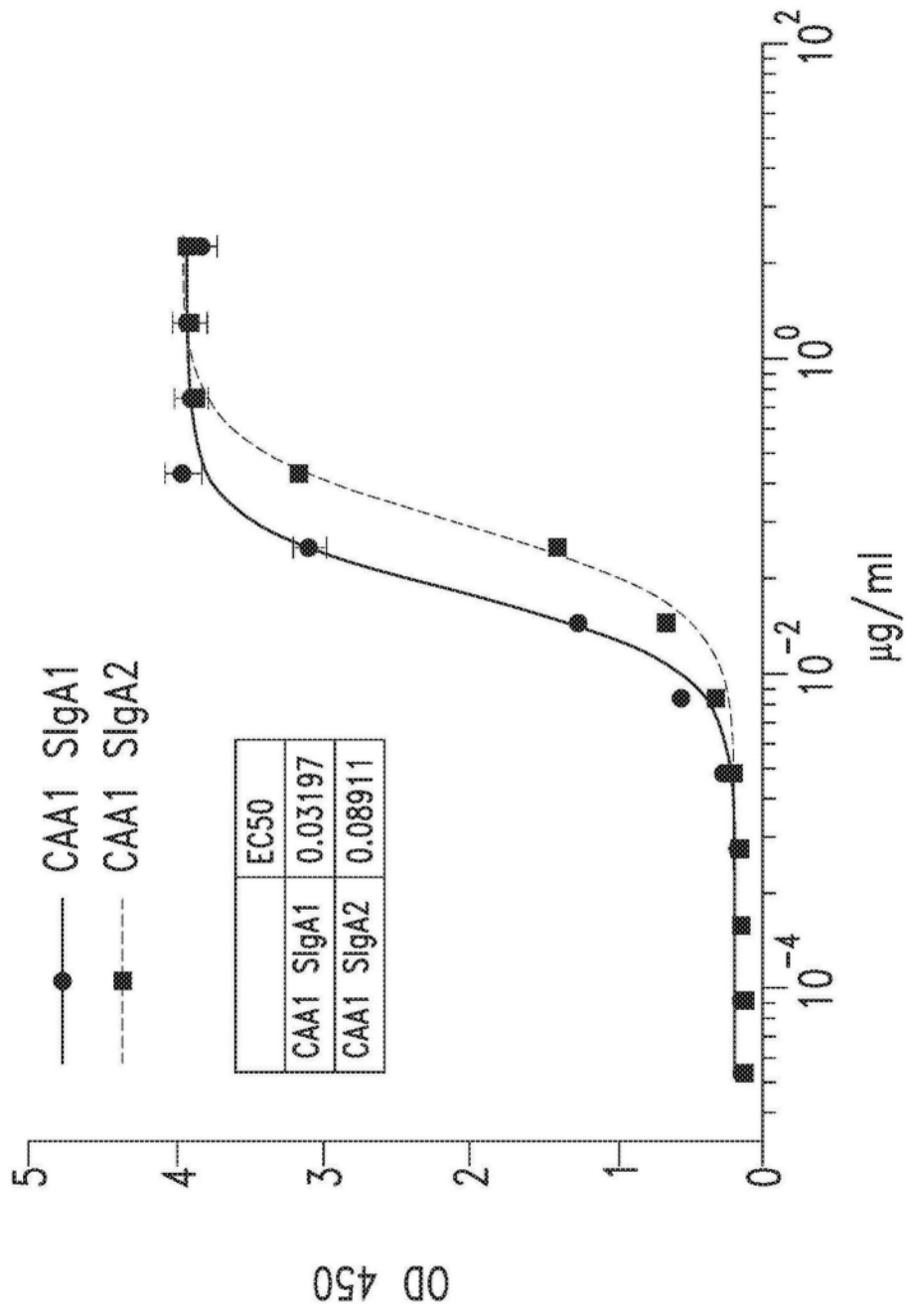


图16B

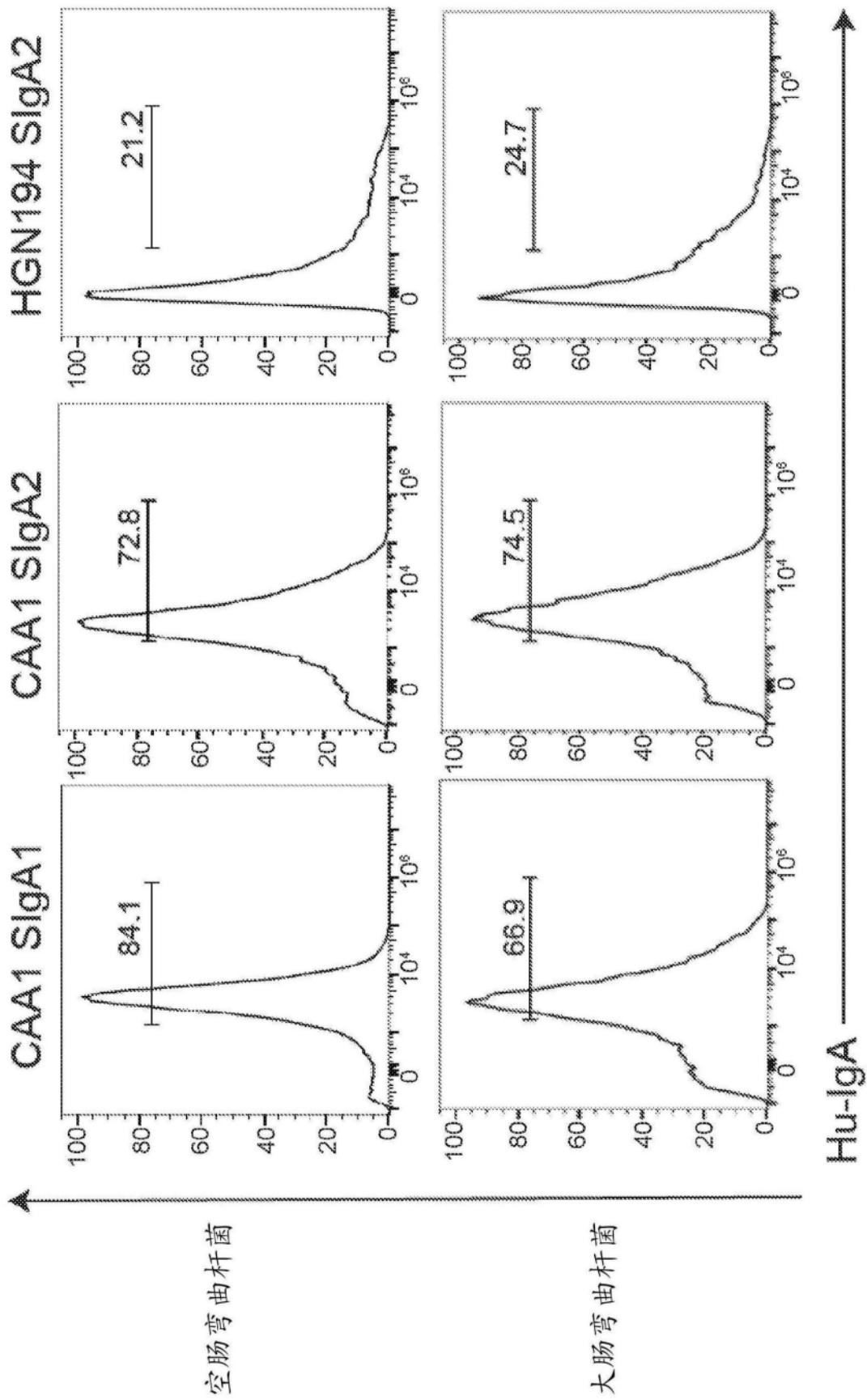


图16C

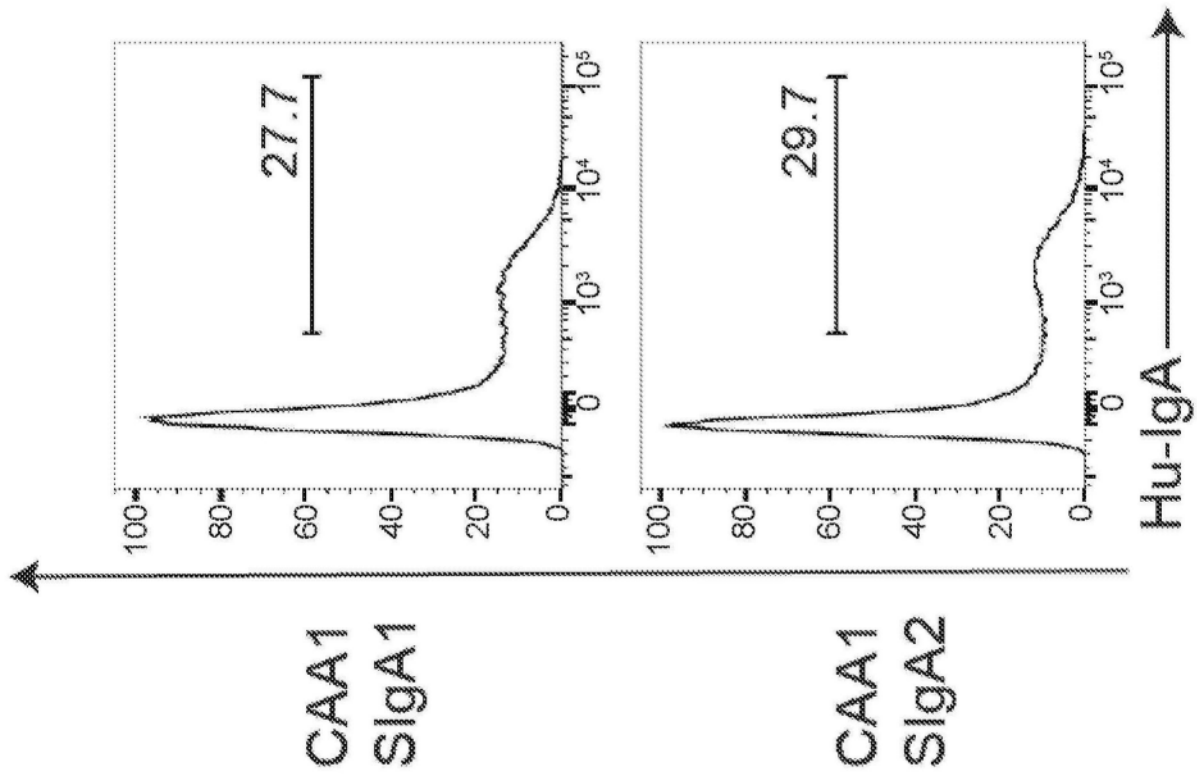


图16D

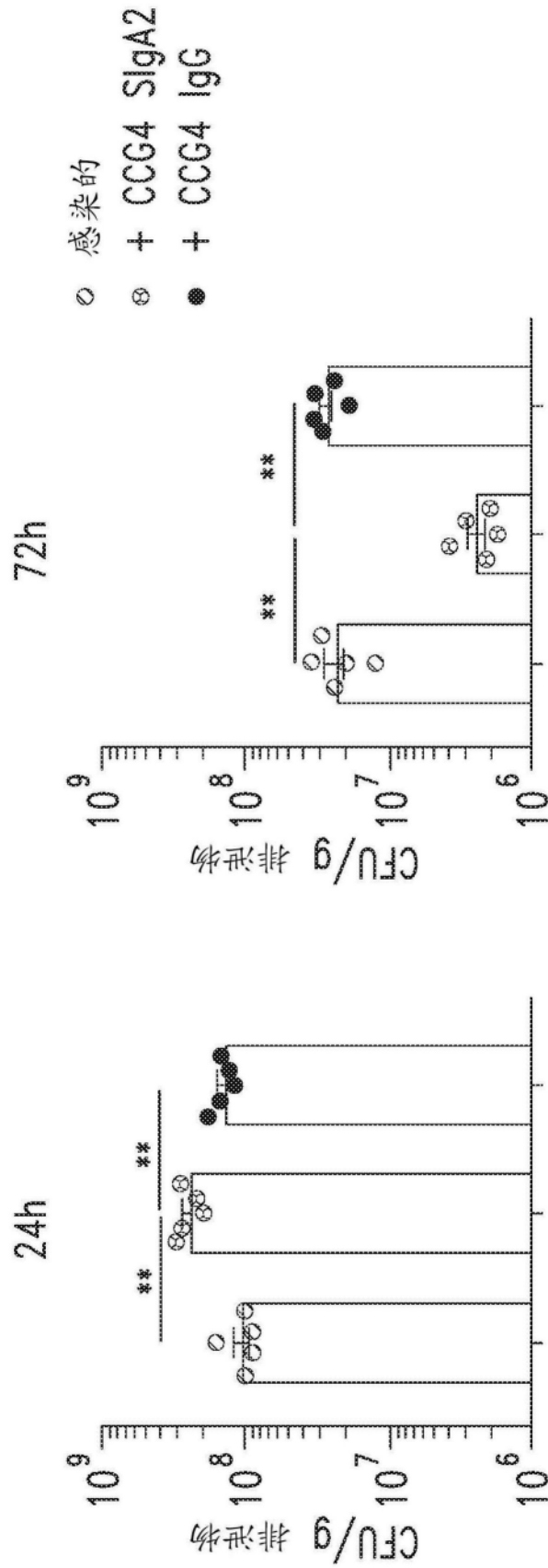


图17A

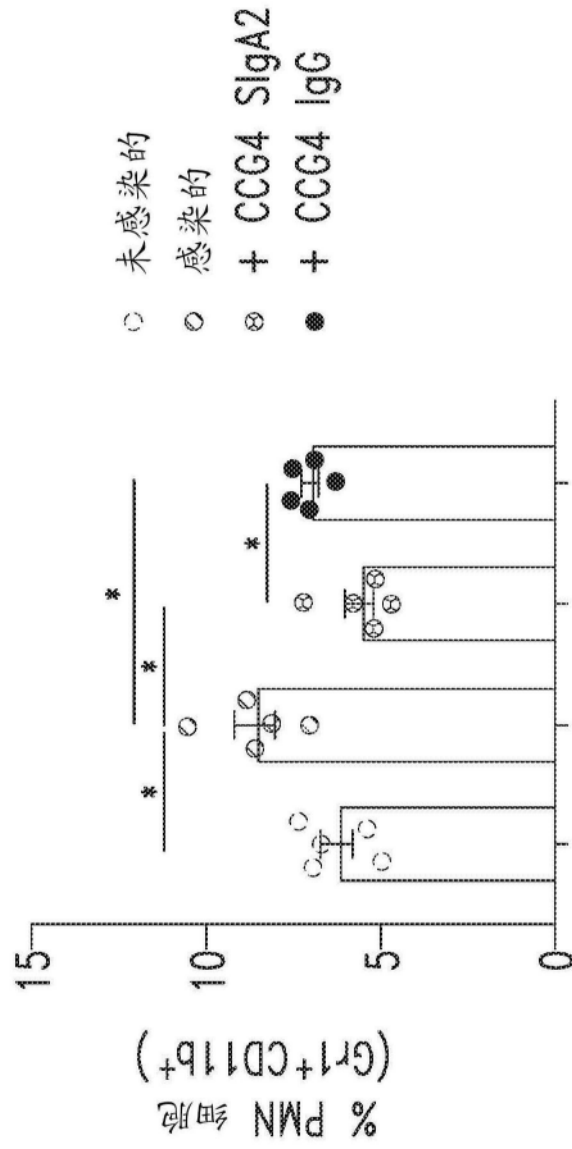


图17B

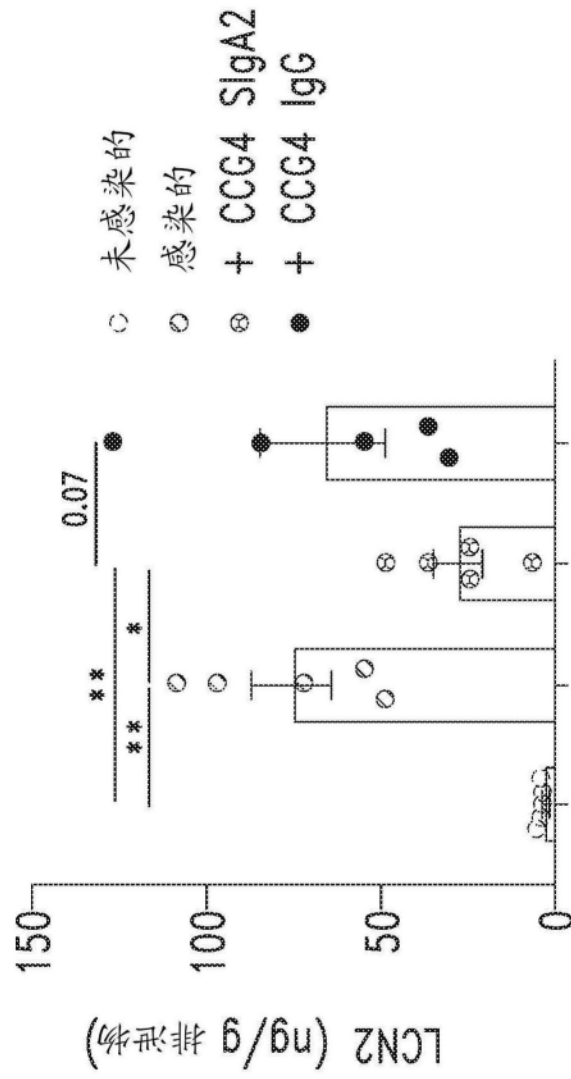


图17C

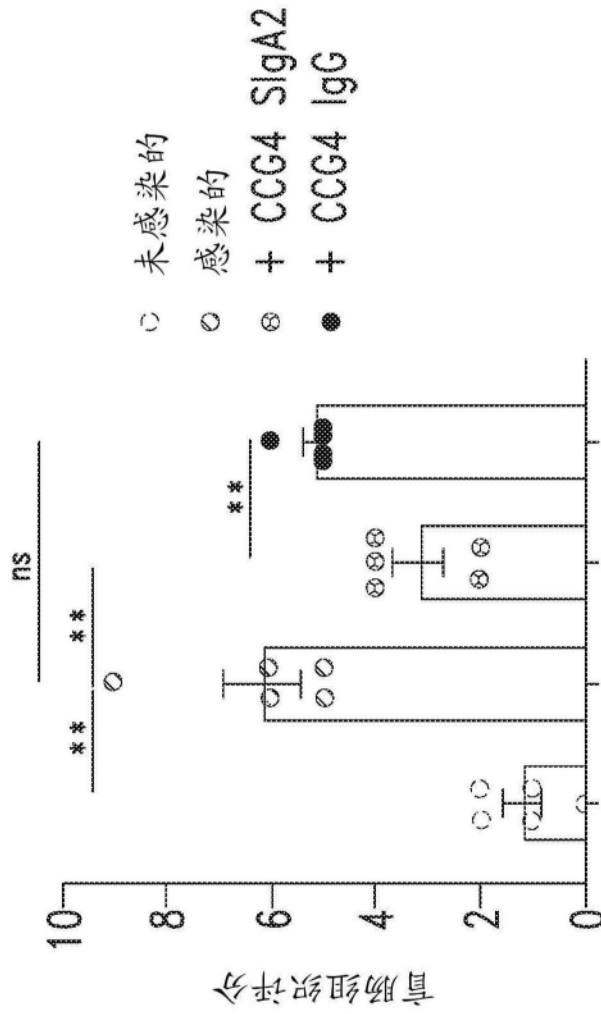


图17D